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Commission of Inquiry on the Blood System in Canada

FINAL REPORT
— Volume 1 —

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The Honourable
Mr Justice Horace Krever

Commission of Inquiry
on the Blood System
in Canada



This Final Report consists of three volumes. The table of contents in each volume is complete for that volume and abbreviated for the other two volumes.

Commission of Inquiry on the Blood System in Canada

FINAL REPORT
— Volume 1 —

The Honourable
Mr Justice Horace Krever

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Commission of Inquiry
on the Blood System in Canada



Commission d'enquête
sur l'approvisionnement en sang au Canada

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TO HIS EXCELLENCE
THE GOVERNOR GENERAL IN COUNCIL

MAY IT PLEASE YOUR EXCELLENCE

Pursuant to a commission under the Great Seal of Canada and dated 27 October 1993,
I have inquired into the blood system of Canada and, with this letter, do now transmit my
report.

Respectfully submitted,

A handwritten signature in black ink that reads "Horace Krever".

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Contents

— Volume 1 —

Foreword *xvii*

Acknowledgments *xix*

Some Important Milestones: HIV and AIDS, 1981–94 *xxi*

Some Important Milestones: Hepatitis, 1965–95 *xxix*

PART I Introduction

1 The Scope and Nature of the Inquiry *3*

The hearings *6*

The sequel to the hearings *7*

2 Blood: Blood Components and Blood Products *11*

The immune system *11*

Components of blood *15*

Processing blood to components and plasma products *19*

Transfusions of blood or blood products *24*

Risks in transfusion *29*

HIV and hepatitis C *33*

Acquired immunodeficiency syndrome (AIDS) and
human immunodeficiency virus (HIV) *33*

Hepatitis C and the hepatitis C virus *38*

PART II The Canadian Blood System at the Emergence of AIDS

Introduction *43*

- 3 The Canadian Red Cross Society 44**
 - Developments at the Red Cross 44
 - Developments at Connaught 47
 - Improvement of the blood transfusion service 48
 - The organizational structure of the Canadian Red Cross Society in 1982 51
 - Organizations in the United States 58
- 4 The Search for Self-Sufficiency in Fractionation 60**
 - Fractionation at Connaught 61
 - Red Cross plans for fractionation 62
 - Connaught–Red Cross relations 66
 - The Ad Hoc Federal-Provincial Committee on Plasma Fractionation 68
 - The Chatfield Committee 73
 - Provincial responses 78
 - A joint-venture proposal for fractionation 79
 - Later fractionation contracts 80
 - The Chapin Key Report 84
 - The consequences of conflict 88
- 5 The Canadian Blood Committee and Its Relationship with the Canadian Red Cross Society 90**
 - The relationship between provincial governments and the Red Cross 90
 - Recommendation for the creation of a Canadian blood authority 93
 - The creation of the Canadian Blood Committee 95
 - The Red Cross response to the Canadian Blood Committee's terms of reference 97
 - The secretariat 99
 - The advisory subcommittee 99
 - A national blood policy 102
 - The working relationship between the Canadian Blood Committee and the Red Cross 104
 - Increasing tensions between the Red Cross and the Canadian Blood Committee 106
- 6 The Bureau of Biologics and the Regulation of Blood and Blood Products 111**
 - The organization of the federal regulatory authorities 111
 - The Health Protection Branch 111
 - The Laboratory Centre for Disease Control 113
 - The Field Operations Directorate 114
 - The Drugs Directorate 115

The Bureau of Biologics	115
The Blood Products Division	116
The U.S. regulator	116
The legislative framework	117
The <i>Food and Drugs Act</i>	117
The <i>Food and Drug Regulations</i>	119
Division 8 of Part C of the <i>Food and Drug Regulations</i> : “New Drugs”	121
Division 4 of Part C of the <i>Food and Drug Regulations</i> : Schedule D Drugs	123
The ambit of regulatory control afforded by Division 4	124
Division 4: The general provisions	126
Division 4: Preparations from human sources	128
Division 4: Human plasma collected by plasmapheresis	130
Removing potentially hazardous drugs from the marketplace	132
The limited resources of the Bureau of Biologics	134
Regulatory control of the Red Cross blood transfusion service	136
The actions of the Bureau of Biologics	137
The response of the senior management of the Department of National Health and Welfare	142
The bureau’s use of its regulatory authority	146
7 The Public Health Environment	148
Federal public health bodies	149
Laboratory Centre for Disease Control	149
Advisory Committee on Epidemiology	151
Provincial public health authorities	152
Provincial public health services	152
Health units	154
Notifiable and reportable diseases	155
The process of identifying an emerging disease	156
Public health authorities outside Canada	157
Public health institutions in the United States	158
The World Health Organization	159
The Council of Europe	159
The common perception of public health services in 1982	160
8 The Care and Treatment of Hemophilia	163
The evolution of the treatment of hemophilia	164
The role of the Canadian Red Cross Society	170
The Canadian Hemophilia Society	171
The development of comprehensive-care clinics	174
The extent of home care	176

PART III
*The Canadian Response to Threats to the Safety
of the Blood Supply*

THE EMERGENCE OF AIDS

9 The Recognition of AIDS as a Blood-Borne Disease	181
10 Canada's Early Response to the Emergence of AIDS	195
Early responses by federal and provincial health authorities	195
The response to the first report of AIDS among hemophiliacs	198
The Canadian Red Cross Society	199
The Canadian Hemophilia Society	202
Canadian surveillance studies of AIDS among hemophiliacs	205

AIDS: SAFETY IN BLOOD AND BLOOD COMPONENTS

11 Measures to Reduce the Risk of Contamination	208
Donor recruitment, pre-AIDS	209
Nature of donor questioning and examination in 1982	211
Recruitment pressures	212
December 1982: Growing recognition that AIDS was transmissible by blood	213
January 1983: Adoption by U.S. blood bankers of measures to defer donors at higher risk	218
January–February 1983: Consideration of donor deferral in Canada	224
March 1983: Enhanced donor-screening measures in U.S. blood banks	229
March 1983: Announcement of voluntary self-exclusion in Canada	231
The environment in which self-exclusion was introduced	234
March–April 1983: Consideration of screening measures in Canada	237
May 1983: Creation of the National Task Force on AIDS	243
May–June 1983: Consideration of the level of risk and of confidential unit exclusion	244
July 1983: Communications with representatives of the gay community	247
July 1983: A second press release from the Canadian Red Cross	249

Community-based measures to prevent contamination	252
Vancouver	252
Toronto	253
Winnipeg	255
Halifax	256
Other examples	256
July–December 1983: Plans for a pamphlet about AIDS for prospective donors	257
January 1984: Confirmation of the link between transfusion and AIDS	264
January–May 1984: Publication of the Canadian Red Cross AIDS information pamphlet	265
July–December 1984: Evaluation and continuation of the AIDS pamphlet pilot project	269
January–May 1985: Concerns about use of the pamphlets	272
August 1985–November 1986: Revised Red Cross pamphlets	276
Effectiveness and eventual implementation of confidential unit exclusion	277
Other risk-reduction measures	280
Autologous transfusion	280
Education of physicians	281
Avoidance of high-risk groups in donor recruitment	281
Evaluation of surrogate tests	282
Commentary	282
Measures taken in the United States to reduce the risk of contamination	284
Measures taken to discourage high-risk donors in Canada	286
Competing concerns	292
Assessment of risk	294
12 The Introduction of Testing for HIV Antibody	297
April 1984: Identification of the virus	299
August 1984: Preparations for HIV-antibody testing	301
October 1984–January 1985: A Canadian study of HIV testing	306
February 1985: Evaluation of test kits	308
March 1985: Licensing of test kits in the United States; recommendations for action in Canada	309
April 1985: The Red Cross's plan for testing	313
May 1985: Preparations for implementation; involvement by the provinces	316
June and July 1985: Delays in funding	317
August 1985: Approval of funding	323
Alternative test sites	324
The consequences of delay in testing	328

Commentary	330
Phase 1: Consultation with the National Advisory Committee on AIDS	331
Phase 2: Funding by the Canadian Blood Committee	332
Phase 3: Implementation Period	335
Provincial testing for HIV antibody	336
13 Notifying the Recipients of Contaminated Blood and Blood Components	338
Recipient notification before the implementation of HIV-antibody tests	339
Sharing of information between public health agencies and blood centres	342
Issues of notification raised by implementation of HIV-antibody testing	345
HIV-antibody testing and recipient notification in Canada	347
Early public information campaigns	350
Development of a policy about recipient notification	351
Public announcements to all recipients	354
Look-backs at some Red Cross blood centres	356
Failure of look-backs and the need for testing all recipients of blood components	360
Hospital for Sick Children study and subsequent public announcements	361
The stored samples	363
Commentary	364

— Volume 2 —

AIDS: SAFETY IN BLOOD PRODUCTS

14 The Risk in Factor Concentrates	367
15 The Conversion to Heat-Treated Concentrates	415
16 Safety in Heat-Treated Concentrates	484
17 The Decline of the Domestic Fractionation Industry	526
18 Treatment of Hemophiliacs in the Era of AIDS	533

AIDS: RESPONSES OUTSIDE THE BLOOD PROGRAM

- 19 The Public Health Authorities: Information about AIDS 548
20 Contact Tracing 573
21 The Risk to the Sexual Partners and Children
of Hemophiliacs 591

HEPATITIS: SAFETY IN BLOOD COMPONENTS AND BLOOD PRODUCTS

- 22 The Nature and History of Hepatitis 612
23 Surrogate Testing 628
24 Canada's Rejection of Surrogate Testing 649
25 The Canadian Response to Post-Transfusion Hepatitis:
Commentary 687

CONSEQUENCES

- 26 The Consequences of the Contamination of
the Blood Supply 708

— Volume 3 —

PART IV
*International Responses to the Risk of
HIV in the Blood Supply*

- Introduction 721
International Milestones: HIV and AIDS, 1981–8 724
27 The United States 734
28 Australia 788
29 France 807

- 30 Germany 842
- 31 Japan 880
- 32 The Netherlands 898
- 33 The United Kingdom 923
- 34 Comparative Tables 946

PART V
Safety of Plasma Derivatives

- 35 Safety of Plasma Derivatives: The Role of Regulation 955

PART VI
Towards a New Blood System

- 36 The Blood Supply System in Canada:
Systemic Problems in the 1980s 985
- 37 The Need for Reform of the Current System 1002
- 38 The Initiative of the Federal, Provincial, and Territorial
Governments to Reform the Blood System 1023
- 39 Financial Assistance for Blood-Associated Injury 1029
- 40 The Blood System for the Future 1046

Afterword 1075

Appendices

- A Government of Canada Commission
Ontario Commission
Prince Edward Island Order-in-Council
Saskatchewan Order-in-Council 1079
- B Commissioner and His Staff 1096

- C Rules of Procedure and Practice for the Commission of Inquiry into the Blood Supply 1098
- D Parties Granted Standing and Their Counsel 1106
- E Intervener Funding; Order in Council and Annex "A" – Guidelines 1109
- F Persons Appearing before the Inquiry 1113
- G Public Submissions to the Commission 1129
- H Interim Report Recommendations 1131
- I Inquiry Schedule 1136

Foreword

In the pages that follow, an account is given of a public health disaster that was unprecedented in Canada and, if we have learned from it, one that will never occur again. The account rightly directs attention to the multitude of our fellow members of Canadian society who suffered the loss of health and life as a direct result of the disaster.

It would be unreasonable, however, to fail to commend two groups of persons whose contributions to the well-being and preservation of the lives of countless members of the Canadian public might otherwise be obscured by the enormity of the tragedy that this Report describes. The first group is that of the blood donors, about whom I said in the Interim Report:

Earlier I referred to the beneficence of the generous group of Canadian blood donors who are the heart of the blood system. All members of Canadian society, and not merely the direct beneficiaries of their generosity, owe the donors a debt that can never be repaid. They are truly life savers. It is important that I emphasize that nothing I have recommended will diminish the urgent need for donations. The history of their humanitarian action persuades me that the blood donors of Canada can be relied on to continue their selfless benefactions as long as blood is necessary for therapeutic purposes.

The second group consists of the front-line Red Cross workers, both employees and volunteers, whose essential services and dedication brought to reality the generous intentions and expectations of the blood donors.

Acknowledgments

An undertaking of the magnitude and complexity that characterized this Inquiry, though conducted by a single commissioner, cannot be carried out without the dedication and untiring work of an excellent team. It was my good fortune to be able to persuade very able persons, whose names are listed elsewhere in this Report, to interrupt their regular careers and become members of the team. Their competence was matched by their loyalty and their intense concern for the public welfare. I am grateful to them all.

Special mention must be made of a few of my colleagues in this enterprise. Earlier experience had taught me that the most important decision a commissioner makes is his or her choice of counsel. I was immensely relieved when, having determined to have the best, my first choices accepted my invitation. They were Marlys Edwardh and Céline Lacerte-Lamontagne. M^e Lacerte-Lamontagne, now the Honourable Judge Lacerte-Lamontagne, acted as counsel until her appointment to the Court of Quebec in December 1994. She was succeeded by Roy Stephenson who, in turn, was succeeded by Melvyn Green, who served from April 1995 until the end. All of them served with distinction and in the best traditions of the legal profession. Ms Edwardh acted not only as chief counsel but also, in effect, as chief of staff. It is impossible to discharge the debt the public owes her. Ms Edwardh and M^e Lacerte-Lamontagne were ably assisted by Delmar Doucette, Frédéric Palardy, Leslie Paine, and Louis Sokolov.

Invaluable advice and assistance in matters scientific and, indeed, in general, were given to me, first, by Dr George E. Connell, O.C., and, later, until the conclusion of the Inquiry, by Dr Penny Chan. I was the grateful beneficiary of the experience and diplomacy of my able administrator, Mary Ann Allen. My editors laboured under intense pressure with excellent results. Ian Montagnes's general advice was as important and helpful as his editorial services. Rosemary Shipton, Mary McDougall Maude, Dan Liebman, Thérèse de la Bourdonnaye, Marie-Joëlle Auclair, and Nicole Henderson, working under trying conditions, demonstrated skills I did not know editors had.

At various times throughout the Inquiry and, in some cases, at all times, I received advice, help or encouragement, and often all three, from many persons. At the inevitable risk of inadvertently omitting names that should be included, I express my gratitude to the following persons: Dr Robert Abels;

Dr Geoffrey Anderson; Dr Thomas Asher; Dr Maung T. Aye; Mr Justice J.-L. Baudouin; Dr John Bowman; Dr Michael Brain; Mr Martin Bruce; Dr Conrad Brunk; Dr Reinhard Burger; Dr Michael Burgess; Mr John Burns; Mr Justice R.M. Carr; Dr John Cash; Dr Michel Chrétien; Dr Donald Cowan; Mrs Marie Crookston; Dr David Davis; Mr M. Decter; Dr John Dick; Professor Bernard Dickens; The Honourable Charles L. Dubin; Ms Jutta Etzler; Dr Donald Francis; Dr Mark Greenberg; Dr Barend G. Grobbelaar; Dr Allan Gross; Dr Gershon H. Growe; Dr Harold Gunson; Dr John E.F. Hastings; Dr Paul Hébert; Professor T.G. Ison; Dr Louis Jacques; Mr Jon Johnson; Dr Peter Jones; Dr Kevin Kain; Dr Rima Khabahz; Dr Alexander H. Klein; Dr John Langstaff; Dr Frederick H. Lowy; Dr Tak Mak; Dr Richard Mathias; Dr Kenneth McClatchey; Dr Stephen McColl; Dr Ernest A. McCulloch; Dr Timothy L. McDaniels; Ms Krista McKerracher; Dr James W. Mosley; Dr William Noble; Dr Alex Proudfoot; Dr David A. Reichman; Dr Robert S. Remis; Dr David Rosencrantz; Mr Justice M.L. Rothman; Dr Michael Shannon; Dr John Shortreed; Dr Margaret Somerville; Dr Richard Spence; Dr B.P. Squires; Dr Moshe Sternberg; Dr Faith Stratton; Dr Susan Tamblyn; Dr Michael Thomas; Dr Marie Trudel; Dr Willem G. van Aken; Mr. David Wiesner; Dr Thomas F. Zuck.

Some Important Milestones: HIV and AIDS, 1981–94

1981

- June First published report of homosexual men in the United States infected with *Pneumocystis carinii* pneumonia (a sign of AIDS). *Morbidity and Mortality Weekly Report*
- July Ten new cases of *Pneumocystis carinii* pneumonia and twenty-six cases of Kaposi's sarcoma (a sign of AIDS) are diagnosed in homosexual men. *Morbidity and Mortality Weekly Report*
- December First published report of *Pneumocystis carinii* pneumonia in intravenous drug abusers. *New England Journal of Medicine*

1982

- March First published report of a homosexual man in Canada infected with *Pneumocystis carinii* pneumonia. *Canada Diseases Weekly Report*
- June A cluster of cases of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia among American homosexual men is reported, providing support to the theory that the disease is caused by an infectious agent. *Morbidity and Mortality Weekly Report*
- July Three hemophiliacs in the United States who had been treated with factor VIII concentrate are diagnosed with *Pneumocystis carinii* pneumonia. *Morbidity and Mortality Weekly Report*
- The United States Public Health Service creates a Task Force on Opportunistic Infections in Hemophilia Patients to determine whether the use of blood products is a risk factor for AIDS.
- August Eight cases of AIDS are reported to the Health Protection Branch in Canada. Officials in the Bureau of Biologics ask the Canadian Red Cross and the Canadian Hemophilia Society to monitor the disease among hemophiliacs.

- October Twelve cases of AIDS are reported in Canada: seven homosexual men, five persons from Haiti, and one person from Africa (one case fell into two groups). *Canada Diseases Weekly Report*
- The U.S. National Hemophilia Foundation passes a resolution that plasma not be collected from homosexual men, intravenous drug abusers, and persons who had resided in Haiti.
- December Four new cases of AIDS in hemophiliacs and one case of transfusion-associated AIDS in an infant are reported in the United States. *Morbidity and Mortality Weekly Report*
- It is reported that a Montreal study has concluded that hemophiliacs who had been treated with factor VIII concentrate have immune deficiencies similar to those of non-hemophilic patients infected with AIDS. *Canada Diseases Weekly Report*
- The U.S. Food and Drug Administration recommends that fractionators refrain from collecting plasma from donors at high risk of contracting AIDS.
- Alpha Therapeutic Corporation, a U.S. fractionator, introduces a donor-screening program to exclude plasma donors at high risk of contracting AIDS.
- The U.S. National Hemophilia Foundation recommends in its medical bulletin that mild hemophiliacs, newly diagnosed hemophiliacs, and hemophiliacs under the age of five years not be treated with factor concentrates.

1983

- January It is recommended in an editorial in the *New England Journal of Medicine* that hemophiliacs be treated with cryoprecipitate, instead of factor VIII concentrate, to reduce the risk of contracting AIDS.
- The U.S. Public Health Service holds a public meeting, attended by organizations involved in the blood supply, to discuss ways to prevent transmission of AIDS through blood components and blood products. It is agreed that measures should be taken to exclude persons at high risk of contracting AIDS from making blood donations.
- The American Association of Blood Banks, the American Red Cross, and the Council of Community Blood Centers make a joint statement recommending that specific measures, including the use of autologous blood, education of physicians regarding

blood use, and questioning of donors to detect symptoms of AIDS or exposure to patients with AIDS, be taken to reduce the risk of AIDS to the blood supply.

The medical and scientific advisory council of the U.S. National Hemophilia Foundation recommends to manufacturers of factor VIII concentrate, to blood centres, and to physicians treating hemophiliacs that measures be taken to reduce the risk of AIDS to the blood supply.

The American Blood Resources Association recommends that organizations involved in the collection of plasma used in the manufacture of blood products introduce measures to discourage donation by persons at high risk of contracting AIDS.

March

The U.S. Food and Drug Administration recommends to all facilities involved in the collection of whole blood and plasma that donors at high risk of contracting AIDS be instructed not to make donations. All prospective donors are to be asked specific questions to detect AIDS symptoms and exposure to persons infected with AIDS.

In the United States, the distribution of pamphlets on AIDS to donors at blood and plasma centres begins.

The Hyland Therapeutics Division of Travenol Laboratories Inc. (Hyland) is the first U.S. fractionator to receive a licence from the U.S. Food and Drug Administration to market dry heat-treated factor VIII concentrate.

The medical and scientific advisory committee of the Canadian Hemophilia Society distributes to the Canadian Red Cross, the Canadian Blood Committee, and physicians treating hemophiliacs recommendations aimed at reducing the risk of exposure to AIDS for hemophiliacs.

The Canadian Red Cross issues a press release that asks persons at high risk of contracting AIDS not to donate blood.

May

Dr Luc Montagnier and colleagues at the Pasteur Institute in Paris isolate a new retrovirus, lymphadenopathy-associated virus (LAV), believed to cause AIDS.

The National Task Force on AIDS (later the National Advisory Committee on AIDS), a group of scientific and medical experts appointed by the Canadian Minister of National Health and Welfare to provide advice to the Minister on issues relating to AIDS, meets for the first time.

- June First published report of a case of AIDS in a Canadian hemophiliac. *Canada Diseases Weekly Report*
- The Council of Europe recommends that information on AIDS be distributed to blood donors, that physicians and hemophiliacs be informed of the risks of using blood and blood products, and that coagulation factor products be prepared from small pools of plasma.
- July The Canadian Red Cross issues a second press release asking individuals at high risk of contracting AIDS not to donate blood.
- September The Canadian Red Cross learns that an infant in Quebec contracted AIDS from a blood transfusion.
- November The dry heat-treated factor VIII concentrate manufactured by Hyland is licensed in Canada.
- 1984**
- January Eighteen U.S. cases of AIDS believed to be caused by the transfusion of blood components are reported. *New England Journal of Medicine*
- First published report of a spouse of a hemophiliac contracting AIDS. *Annals of Internal Medicine*
- March By this time, all U.S. fractionators include a warning about AIDS on the product inserts for factor concentrates made from U.S. plasma.
- April Dr Robert Gallo announces that he and his colleagues at the U.S. National Cancer Institute have isolated the retrovirus that causes AIDS, the human T-cell lymphotropic virus III (HTLV-III). The U.S. Secretary of Health announces that the cause of AIDS has been identified and that a test will be available within six months.
- April–July The Cutter Biological Division of Miles Laboratories Inc. (Cutter) and five blood banks in the San Francisco Bay area introduce a test for the antibody to the core of the hepatitis B virus as a surrogate test for AIDS.

- May The first Canadian Red Cross pamphlet on AIDS is distributed to donors at blood centres. The pamphlet identifies persons at high risk of contracting AIDS and asks those persons to refrain from donating blood.
- July Ninety-six cases of AIDS are reported in Canada – 60 per cent homosexual or bisexual men, 27 per cent recent immigrants from Haiti, 2 per cent hemophiliacs, 1 per cent intravenous drug abusers, and 10 per cent unclassified cases. *Canada Diseases Weekly Report*
- August The Laboratory Centre for Disease Control announces it will perform diagnostic tests for the presence of antibody to HIV.
- September The first Canadian case of transfusion-associated AIDS in an adult is reported to the Laboratory Centre for Disease Control. It is reported that heat treating factor VIII concentrate can inactivate retroviruses. *The Lancet*
- October It is reported that heat treating factor VIII concentrates can inactivate HIV. *Morbidity and Mortality Weekly Report*
- November The dry heat-treated factor VIII concentrate manufactured by Cutter is licensed in Canada. The Bureau of Biologics directs the Canadian Red Cross to replace non-heat-treated factor concentrates with heat-treated factor concentrates as soon as possible.
- December The Canadian Blood Committee holds a consensus conference, attended by the Canadian Red Cross, Canadian fractionators, the Bureau of Biologics, and the Canadian Hemophilia Society, on the conversion to heat-treated factor concentrates. The results of a study by Dr Christos Tsoukas and colleagues on Canadian hemophiliacs, in which half the subjects in the study were found to be HIV-antibody positive, is published. *New England Journal of Medicine*
- 1985**
- March The U.S. Food and Drug Administration grants licences to distribute HIV-antibody test kits.

	The task force on HIV-antibody testing of the National Advisory Committee on AIDS recommends that the Canadian Red Cross prepare a plan to test all blood donations for the presence of HIV antibody.
April	<p>The medical and scientific advisory committee of the Canadian Hemophilia Society develops a priority list for the distribution of heat-treated factor concentrates until a supply of heat-treated concentrates sufficient for all hemophiliacs is obtained.</p> <p>The medical and scientific advisory committee of the Canadian Hemophilia Society develops "a safe sex advisory" for hemophiliacs and their families.</p>
May	<p>The first Canadian case of transfusion-associated HIV is officially reported.</p> <p>By this time, almost all blood and plasma centres in the United States are testing donations for the presence of HIV antibody.</p>
July	<p>All factor concentrates distributed in Canada are heat treated to inactivate HIV.</p> <p>The first federal-provincial meeting on AIDS is held. HIV-antibody testing of blood donations by the Canadian Red Cross and the establishment of alternative test sites by the provinces are discussed.</p> <p>The U.S. Food and Drug Administration recommends that blood and plasma centres conduct look-backs.</p>
August	The Canadian Blood Committee approves funding for HIV-antibody testing of blood donations.
November	All blood donations in Canada are tested by the Red Cross for the presence of HIV antibody.
1986	
May	It is reported that dry heat treatment of factor concentrates at 60°C may not effectively inactivate HIV. <i>The Lancet</i>
June	The American Association of Blood Banks, the American Red Cross, and the Council of Community Blood Centers issue a joint statement recommending that recipients of untested donations obtained from persons who subsequently are found to be HIV-antibody positive seek testing.

- August** Wet heat-treated factor VIII concentrate, believed to be safer than dry heat-treated concentrate, is first licensed in Canada.
- October** Dry heat-treated factor VIII concentrate manufactured by the Armour Pharmaceutical Company (Armour), using the 60°C process, is withdrawn in the United Kingdom.
The Canadian Red Cross urges that Armour's dry heat-treated factor VIII concentrate be withdrawn. The Bureau of Biologics advises the Red Cross to continue distributing Armour's factor concentrates.
- 1987**
- March** The American Association of Blood Banks, the American Red Cross, and the Council of Community Blood Centers support the recommendation of the Centers for Disease Control that patients who received a blood transfusion between 1978 and April 1985 seek HIV testing.
- Autumn** The Canadian Red Cross establishes a look-back policy.
- October** Six hemophiliacs in British Columbia who had been treated with Armour's dry heat-treated factor concentrate are reported to have contracted HIV; two other hemophiliacs in western Canada treated with the same product are reported to have contracted HIV later in 1987.
- December** The Health Protection Branch announces a recall of three lots of Armour's dry heat-treated factor VIII concentrate identified as directly implicated in the HIV infection of the hemophiliacs in western Canada.
The Bureau of Biologics directs that dry heat-treated factor concentrates be replaced as soon as possible with wet heat-treated concentrates.
- 1988**
- February** The Canadian Hemophilia Society sponsors a consensus conference on wet heat-treated blood products.
- July** All factor concentrates distributed in Canada are wet heat treated.

1989

December Under the Extraordinary Assistance Program, the Canadian government agrees to compensate persons infected with HIV through blood components and blood products.

1993

May The Nova Scotia government agrees to compensate persons infected with HIV through blood components and blood products and their HIV-positive spouses infected through sexual transmission.

June–September Under the Multi-Provincial/Territorial Assistance Program, the other provinces and the territories agree to compensate persons infected with HIV through blood components and blood products.

Some Important Milestones: Hepatitis, 1965–95

- 1965** Report of the discovery of the “Australia antigen” (later referred to as the hepatitis B surface antigen). *Journal of the American Medical Association*
- 1968** Report of the association between the Australia antigen and serum hepatitis. *Proceedings of the National Academy of Science*
- 1972** The Canadian Red Cross implements hepatitis B surface antigen testing throughout Canada.
- 1974** The existence of a third form of viral hepatitis, later referred to as non-A, non-B hepatitis, is postulated.
- 1981**
- April Report of the results of the transfusion transmitted viruses study predicting that testing blood donations for ALT (a liver function test) would reduce the incidence of post-transfusion non-A, non-B hepatitis by 40 per cent. *New England Journal of Medicine*
- June The U.S. National Heart, Lung, and Blood Institute’s ad hoc committee on ALT testing recommends against the implementation of ALT testing in favour of further study of its efficacy.
- August Report of the results of the U.S. National Institutes of Health’s study predicting that ALT testing of blood donations would reduce the incidence of post-transfusion hepatitis by 29 per cent. *Journal of the American Medical Association*
- November The Canadian Red Cross’s blood transfusion service advisory committee decides that ALT testing of blood donations should not be implemented as a surrogate test for non-A, non-B hepatitis.

1982

- January Report of the results of a study by the Australian Red Cross predicting that anti-HBc (antibody to the core of the hepatitis B virus) testing of blood donations would reduce the incidence of post-transfusion non-A, non-B hepatitis by as much as 50 per cent. *The Lancet*

1984

- July German regulatory authorities require that all blood products distributed for use in Germany be manufactured from ALT-tested plasma.
- December Report of the results of the transfusion transmitted viruses study predicting that anti-HBc testing of blood donations would reduce the incidence of post-transfusion non-A, non-B hepatitis by 33 per cent, and that anti-HBc and ALT testing combined could reduce it by 61 per cent. *Annals of Internal Medicine*

1985

- July Preliminary data from the Toronto incidence study show the incidence of post-transfusion non-A, non-B hepatitis to be 7.6 per cent.
- November The majority of U.S. fractionators begin to use ALT-tested plasma to manufacture blood products.

1986

- February The U.S. Food and Drug Administration's blood products advisory committee recommends that all blood donations for transfusion be tested for both ALT and anti-HBc as surrogate tests for non-A, non-B hepatitis.
- March The American Association of Blood Banks and the American Red Cross issue a joint statement recommending that blood collection agencies begin planning to implement surrogate testing.
- April The American Association of Blood Banks' board of directors decides that both ALT and anti-HBc testing of blood donations should be implemented.

Report of the results from the U.S. National Institutes of Health study predicting that anti-HBc would reduce the incidence of post-transfusion hepatitis by 43 per cent. *New England Journal of Medicine*

The Canadian Red Cross's blood transfusion service advisory committee recommends against surrogate testing for non-A, non-B hepatitis, pending further study of the data from the Toronto incidence study and of the efficacy of HIV-antibody testing as a surrogate test for non-A, non-B hepatitis.

1987

December Dr Blajchman and Dr Feinman submit their application for a grant for a multicentre randomized study of the efficacy of ALT and anti-HBc as surrogate tests for post-transfusion hepatitis to the National Health Research and Development Program.

1988

May Chiron Corporation announces the discovery of a virus (later called HCV) responsible for non-A, non-B hepatitis.

July All factor concentrates distributed in Canada are wet heat treated.

1989

September The Blajchman-Feinman application for a grant for a multi-centre study is accepted by the National Health Research and Development Program and the Canadian Blood Committee.

1990

June The Red Cross implements first-generation HCV-antibody testing.

1991

March The U.S. Food and Drug Administration requires anti-HBc testing of blood donations to identify units contaminated with hepatitis B.

1992

Spring The Canadian Red Cross implements second-generation HCV-antibody testing throughout Canada.

1993

September Dr Blajchman and Dr Feinman present the results of their multi-centre study, which shows that surrogate testing would have significantly reduced post-transfusion hepatitis in Canada before 1990.

1995

January Report of the results of the Blajchman-Feinman multicentre study. *The Lancet*

A U.S. National Institutes of Health Consensus Development Conference statement recommends that volunteer blood donations in the United States no longer be tested for ALT levels, but recommends the retention of anti-HBc testing to detect additional cases of hepatitis B and HIV.

PART I

Introduction

The Scope and Nature of the Inquiry

A nationwide public health calamity occurred in Canada during the late 1970s and the 1980s. The national blood supply was contaminated with two infectious viruses, one causing a newly emerging disease, the other causing a disease that had existed for many years but had not previously been identified precisely. The first of these infectious agents was the human immunodeficiency virus (HIV), which causes acquired immune deficiency syndrome (AIDS). It contaminated the blood supply in the late 1970s and early to mid-1980s. More than 1,000 persons in Canada were infected with HIV through the blood supply, and some unknowingly infected others. The development of AIDS in a person was almost invariably fatal. The second infectious agent was the hepatitis C virus, which infected tens of thousands of persons in Canada through the blood supply. Although the long-term consequences of hepatitis C are not entirely known, it appears that as many as 90 per cent of persons infected with the virus may go on to develop chronic hepatitis and, of these, 10 per cent will develop cirrhosis of the liver or liver cancer after ten years; it appears that after twenty years the proportion increases to 20 per cent.

There were two principal means by which persons became infected with either virus through the blood system. Some were infected after receiving transfusions of blood components (red cells, platelets, or plasma), usually in a hospital and often in the course of surgery. Others became infected after using factor concentrates, blood products used to treat hemophilia, that were made from the pooled plasma of many thousands of donors. Persons with severe hemophilia depended on these blood products for their health and used them as often as several times a week.

The symptoms of AIDS were first recognized in homosexual men in 1981 but little more than one year later were found in three hemophiliacs who had no history of homosexual behaviour. Suspicion was focused immediately on the only element that was common to all their histories, the use of blood products. That suspicion became a certainty in 1984, after the agent causing AIDS, HIV, was identified and a test was developed to detect its presence. At first only available in a few research laboratories, the test later became available on a widespread basis. By 1985 it was clear that many severe hemophiliacs in Canada were infected, and by 1993 it was known that the number

was more than 700. As the 1980s progressed, occurrences were recognized of transmission of the virus through blood transfusions. Some persons who had received transfusions during surgery became ill and learned then that they were infected with HIV. Other persons were identified by the Canadian Red Cross Society (Red Cross) through its records, and were told they might be infected as a result of receiving contaminated blood. Still others learned they were infected after having been tested for HIV antibody, often in the course of applying for life insurance. Some persons who were infected with HIV through blood transfusions still do not know that they are infected.

The risk of transmitting hepatitis through blood had been recognized for many years, and measures had been taken to protect the blood supply from contamination with one form of the disease, hepatitis B. Another form continued to be transmitted through blood and blood products, however, and it was not until 1988 that the agent causing it was identified and a test could be developed to detect its presence. Most persons infected with that form, hepatitis C, did not learn of their infection until the 1990s.

In the late 1980s, many persons infected by HIV from contaminated blood components or blood products sought financial compensation from the Government of Canada. On 14 December 1989, the government announced that it would give \$120,000, tax free and payable in four equal instalments, to all persons infected with HIV through blood components or blood products who would release it from any liability. In May 1993, the government of Nova Scotia announced that, subject to a similar condition, it would give financial assistance to persons infected with HIV from blood, blood components, or blood products; to their spouses if they were infected; and to surviving family members. The other provinces and the territories agreed to give financial support to infected persons in September 1993, on condition that they and others – pharmaceutical companies, hospitals, insurance companies, health care givers – were released from any liability.

By the early 1990s, several hundred Canadians infected with HIV had developed AIDS. Many had already died. Others who had received a blood transfusion in the early 1980s were learning that they were infected with HIV. There was a growing recognition of the extent and gravity of the contamination of the blood supply; questions were raised about how it had occurred, and concerns were expressed about the possibility of a similar contamination in the future. Many infected persons asked for an investigation into the events that had led to the contamination of the blood supply and into the supply's current safety. The subcommittee on health issues of the parliamentary Standing Committee on Health and Welfare, Social Affairs, Seniors, and the Status of Women held hearings between November 1992 and April 1993 to determine the circumstances surrounding the contamination of blood, blood components, and blood products, and to reassure the Canadian public of the safety of the blood transfusion system.

On 13 May 1993, the standing committee submitted a report entitled “Tragedy and Challenge: Canada’s Blood System and HIV” that said that the Canadian blood system “did not respond to the HIV/AIDS challenge as quickly as it might have.” The committee was unable to determine the precise reasons for delay. In particular, it said, there were many unanswered questions with respect to two key events. The first was the introduction of a test for HIV antibody as a means of screening blood donations for HIV. The second was the introduction of blood products that had been heat treated to inactivate HIV in order to reduce the risk of infection. The committee reported that public confidence in the safety and efficiency of the blood system had been seriously shaken. It recommended that a comprehensive review of the Canadian blood system, in the form of a public inquiry, be done “in part to fully clarify the tragic events of the 1980s, in part to reaffirm public confidence in the system, and in part to ensure that the Canadian blood system will be able to deal with future challenges as well as the myriad requirements of day-to-day operations.”

On 16 September 1993, the federal, provincial, and territorial ministers of health, except for the Minister of Health of Quebec, recommended that a public inquiry be established.

Order in Council PC 1993-1879, which provided that a Commission be issued under Part I of the *Inquiries Act* appointing me to undertake this Inquiry, was issued on 4 October 1993. The Commission, which was issued on 27 October, appointed me

to review and report on the mandate, organization, management, operations, financing and regulation of all activities of the blood system in Canada, including the events surrounding the contamination of the blood system in Canada in the early 1980s, by examining, without limiting the generality of the inquiry,

- the organization and effectiveness of past and current systems designed to supply blood and blood products in Canada;
- the roles, views, and ideas of relevant interest groups; and
- the structures and experiences of other countries, especially those with comparable federal systems.

Similar instruments, with the same terms of reference, were issued by the governments of Ontario, Saskatchewan, and Prince Edward Island, appointing me to be a Commissioner under their respective provincial inquiries acts in recognition of the fact that some of the matters under investigation may fall within provincial jurisdiction.

The Commission directed me to submit an interim report “on the safety of the blood system, with appropriate recommendations on actions that might be taken to address any current shortcomings.” The Interim Report

was submitted to the Governor in Council on 15 February 1995. For convenience, the recommendations contained in that report are reproduced in Appendix H.

The Commission also directed me to submit a final report

with recommendations on an efficient and effective blood system in Canada for the future including:

- its managerial, financial, and legal principles as well as the medical and scientific aspects;
- the appropriate roles and responsibilities of the provincial/territorial and federal governments, the Canadian Red Cross Society, and other relevant organizations;
- the contractual and other relationship which should exist amongst the governments and organizations involved in the system;
- resource implications, including current allocations;
- powers that are appropriate to recommendations concerning responsibilities and authorities; and
- actions required to implement these recommendations.

The hearings

Organizational hearings were held in Ottawa on 22 and 23 November 1993. At those hearings the following parties received standing: the Red Cross; the Canadian Blood Agency; the governments of Canada, nine provinces, and the territories; Connaught Laboratories Limited; Miles Canada Inc. (later Bayer Inc.); and nine organizations, including the Canadian Hemophilia Society and the Canadian AIDS Society, representing persons who had been infected with HIV or hepatitis C by blood, blood components, or blood products, and other persons interested in the contamination of the blood supply in the 1980s. Two other organizations representing persons who had been infected and the Association of Hemophilia Clinic Directors of Canada subsequently received standing. The government of the province of Quebec did not seek standing. It participated, and was represented by counsel, in the hearings that took place in Quebec in September 1994 and in the hearings that took place between March and December 1995 in Toronto. All persons, organizations, governments, and counsel who took part in the Inquiry are listed in Appendix D.

The collection of documents began in 1993 and continued throughout the course of the Inquiry. Approximately 175,000 documents, totalling between 800,000 and 1,000,000 pages, were collected. All were read and catalogued. Approximately 19,750 documents were filed as exhibits. Most of the documents were bound into 436 exhibit briefs that were distributed to all persons and organizations with standing.

Early in the Inquiry, I undertook to hear from any person in Canada who had been infected with HIV or with the virus causing hepatitis C as a result of contaminated blood components or blood products, or from members of their families, who wished to relate their experiences to me. Many of these persons were already seriously ill. In order to hear from them and other concerned persons, the first phase of the public hearings was conducted between February and December 1994 in every province except Prince Edward Island, for which evidence was heard in Halifax. In addition to infected persons or members of their families, those who testified in the first phase of the hearings included employees of local Red Cross blood centres, provincial government officials, and representatives of community and AIDS-related organizations. Three hundred and fifteen witnesses testified during this phase of public hearings.

The second phase of public hearings addressed broader national issues concerning the historical actions and relationships of the participants in the Canadian blood system. These hearings took place in Toronto between March and November 1995. Eighty-four witnesses testified during more than 100 days of hearings.

The third phase of public hearings addressed the organization of the current blood system. In this phase of the hearings, which took place in Toronto during November and December 1995, round table discussions were held on issues affecting the current blood system; case studies were conducted with the cooperation of the major organizations in the system – the Canadian Red Cross Society, the Canadian Blood Agency, the Government of Canada, the Canadian Hemophilia Society, and the Association of Hemophilia Clinic Directors of Canada – to examine what changes had been made to their decision-making processes since the 1980s; and presentations were made by the major organizations regarding the current blood system.

Throughout the course of the Inquiry, I heard from 474 persons during the 247 days of hearings. I received written submissions from eighty-nine persons and organizations with an interest in the blood system, including many who did not have standing. In addition, more than 300 persons called a toll-free telephone number that was opened so that any person in Canada could speak to me or a member of my staff in either of Canada's official languages. The testimony and submissions produced 50,011 pages of transcript, and 1,303 exhibits consisting of nearly 100,000 pages. A list of the witnesses appearing before the Inquiry is contained in Appendix F. A list of public submissions to the Commission is contained in Appendix G.

The sequel to the hearings

Section 13 of the *Inquiries Act* requires that notice be given to any person about whom comment might be made in the Report that could be interpreted as "misconduct." Although the meaning of misconduct is not defined in the

Act, the Supreme Court of Canada has recently held that misconduct includes “improper or unprofessional behaviour” or “bad management.” In fact, notice was given if any finding or comment might be made that reflected adversely on a person or organization, including anything that negatively affected his, her, or its reputation.

On 21 December 1995, after the completion of the principal hearings, I caused notice to be given confidentially to ninety-five persons, corporations, and governments that I might make findings of fact about conduct in the years in question that might amount to misconduct within the meaning of the *Inquiries Act*. The notice in every case informed the recipient that he, she, or it had a full opportunity to be heard in person or by counsel with respect to the potential findings.

The final phase of hearings was to take place in early 1996 but, before the hearings took place, an application was brought in the Trial Division of the Federal Court of Canada challenging my jurisdiction to make some of the potential findings of fact described in the section 13 notices. The application was heard in May 1996 and dismissed in June 1996. Some of the applicants appealed to the Federal Court of Appeal. In October and November 1996, while the appeal was pending, evidence was heard on behalf of some of the recipients of the section 13 notices. In December 1996, final submissions were heard from the persons and organizations who participated in the hearings and from the recipients of section 13 notices who chose to make submissions. During the same month, the Federal Court of Appeal heard the appeal. Its decision was delivered in January 1997. The appeal of one appellant was allowed; the other appeals were dismissed. Some of the unsuccessful appellants appealed to the Supreme Court of Canada. Their appeals were dismissed on 26 September 1997.

On 22 November 1993, the first day of public hearings, in the course of my introductory comments about the Inquiry, I made the following statement about its purpose:

It is not and it will not be a witch hunt. It is not concerned with criminal or civil liability. I shall make findings of fact. It will be for others, not for the commission, to decide what actions if any are warranted by those findings.

I shall not make recommendations about prosecution or civil liability. I shall not permit the hearings to be used for ulterior purposes, such as a preliminary inquiry, or Examination for Discovery, or in aid of existing or future criminal or civil litigation.

As I interpret the terms of reference, the focus of the Inquiry is to determine whether Canada’s blood supply is as safe as it could be and whether the blood system is sound enough that no future tragedy will occur. For

those purposes it is essential to determine what caused or contributed to the contamination of the blood system in Canada in the early 1980s.

We intend to get to the bottom of that issue, let there be no mistake about that.

Part III of this Report describes "the events surrounding the contamination of the blood supply in the early 1980s." The events did not occur without human intervention. For the most part they were the result of decisions, actions, and inactions by persons, organizations, and governments. In what follows, in my description of events, actions, and inactions, I imply no conclusions or opinions about liability, either civil or criminal. Any inference taken that any such conclusion is made or opinion is held would be wrong. It must also be remembered that the rules of evidence and procedure applied in an inquiry are different from those applied in courts of law. The findings of fact that are made in this Report, therefore, are not necessarily the same as those that would be reached in a court.

Part I of this Report describes the nature and uses of blood and its derivative products and the risks that attend their use. Part II reviews the principal organizations involved in the blood system and their roles in the 1980s, when the first cases of AIDS were reported in Canada. A chapter is devoted to hemophiliacs, a group of Canadians who were uniquely vulnerable to infection through the blood supply because of their unavoidable dependence upon blood products. In Part III, the emergence of AIDS is reviewed briefly, followed by detailed examinations of the measures taken in Canada to protect the safety of blood components and blood products – first, from contamination with the causative agent of AIDS, eventually identified as the human immunodeficiency virus (HIV), and then from contamination with the virus that causes hepatitis C. Part III also includes an examination of responses from outside the blood program, in particular those of the public health authorities. The historical chapters review events that are complex in chronology and in subject matter. The reader may be assisted by reference to two chronologies of important events surrounding the contamination of the blood supply by, respectively, HIV and hepatitis C. Those chronologies begin on pages xxi and xxix. I have also tried to assist the reader by including necessary background information in each chapter, often at the cost of some repetition.

Part IV reviews the measures that were taken to protect the blood supply in seven other countries, representing a variety of types of blood systems. These countries provide a fair representation of both federal and unitary developed nations and present a useful context in which to consider the events surrounding the contamination of the blood supply in Canada. These countries are the United States, Australia, France, Germany, Japan, the Netherlands, and the United Kingdom.

Part V is a discussion of the safety of plasma derivatives. My Interim Report, dated February 1995, concerns the safety of the blood system, but does not include a discussion of this topic because I had insufficient information at that time. I am now in a position to address that issue.

Part VI addresses the future of the blood system. It commences with an analysis of the major systemic problems that contributed to the contamination of the blood supply in the 1980s, followed by discussions of recent changes to the blood supply system that have been undertaken. There is a description of proposals for reform of the system made by the federal and the provincial and territorial governments. Finally, I discuss compensation for those persons injured by blood or blood products, and make a series of recommendations for a new blood supply system.

2

Blood: Blood Components and Blood Products

Long before anyone knew why, it was known that blood is essential for life. Only gradually, beginning in the late nineteenth century, have we come to understand the complex of components and functions that make the role of blood truly vital.

Blood's most important function is delivering oxygen to tissues throughout our bodies. When much blood is lost, there is not enough volume in the system, and the heart stops functioning; it is a pump that has gone dry. Vital organs like the brain and heart shut down within minutes if they are deprived of the oxygen blood carries. But blood has many other vital functions. It carries nutrients from the intestines to the tissues, toxic waste products to the liver and kidneys for breakdown or excretion, and hormones from the glands or organs where they originate to the site where they function. Blood also contains and transports key components of the immune system that protects the body from infection.

To minimize the loss of blood, the body has its own defences. When a blood vessel is broken it constricts, and a blood clot is formed by a process that involves many components in a cascade of interactions.

This Report is concerned with the use of blood in the Canadian health system. Inevitably it involves technical language and some understanding of the nature and functions of blood, the processes by which blood, its components, and blood products are prepared for and used in health care, and the attendant risks to patients' health. This chapter is meant as a brief, and far from comprehensive, introduction to those subjects.

First, several terms must be defined and certain concepts explained.

The immune system

The immune system, its components, and its functions are part of, and closely interrelated with, blood and are therefore fundamental to an understanding of the functions of blood. The immune system is the body's principal defence against foreign material. It is the means by which the body clears itself of

inanimate debris and such infectious microorganisms as bacteria and viruses. Immune functions are activated when foreign material enters the body by penetrating its physical and chemical barriers, such as the skin and the mucous membranes and their secretions. The secretions – sweat, tears, and saliva – serve to wash the surface of the body and contain substances that can kill some infectious microorganisms.

There are two types of immune functions or defences, non-specific and specific.

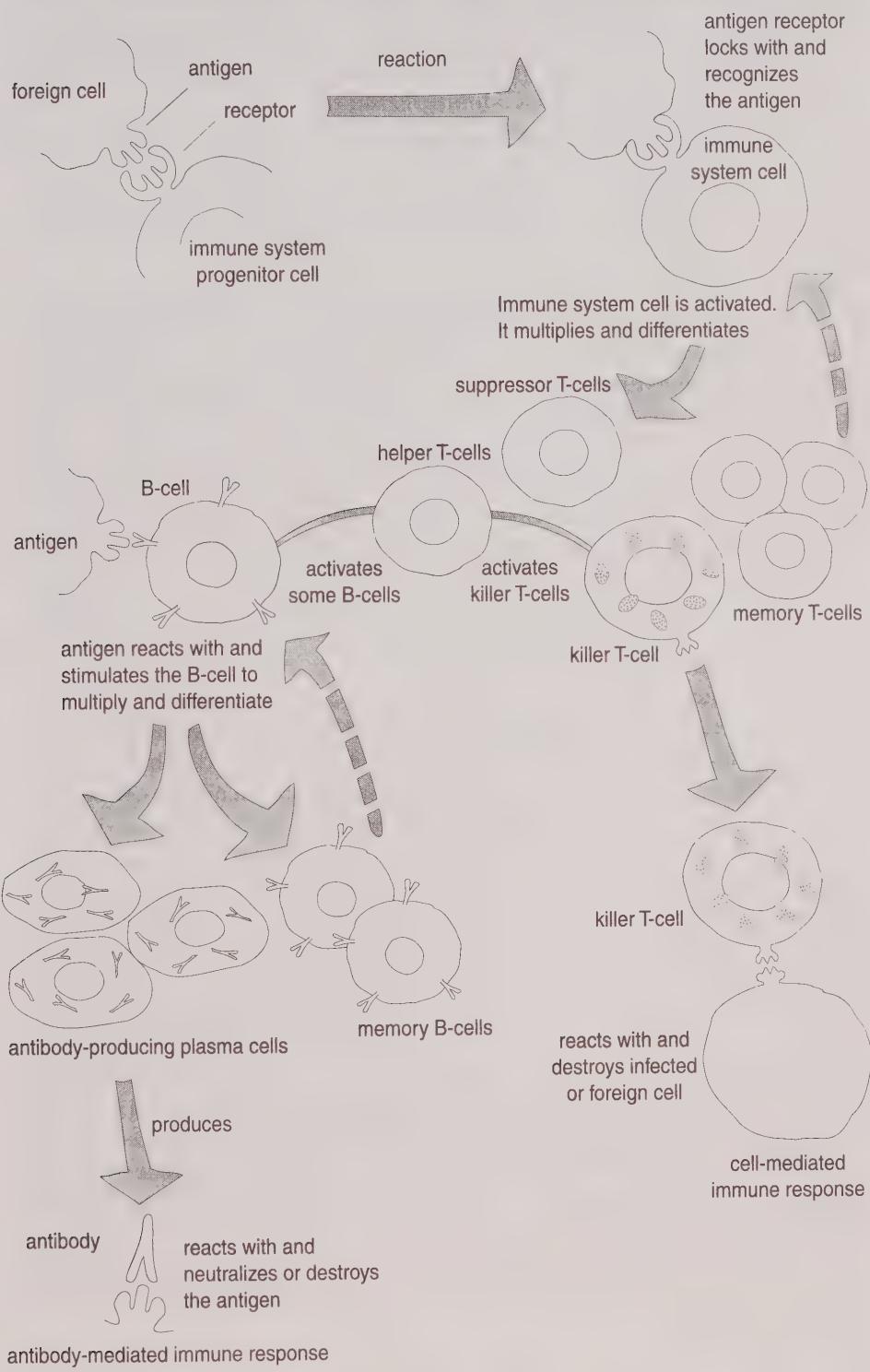
The *non-specific immune functions* involve, among other things, cells that can engulf small particles of material and release chemicals that destroy that material and alert the body to the threat of invasion. These chemicals also cause inflammation by increasing the flow of blood and thus attracting more defensive cells to the area.

The *specific immune functions* are triggered when certain cells identify a particular kind of foreign material and react to it. These cells have receptors on their surface that recognize and bind to *antigens*, which are molecular structures on the surface of the foreign material. The process is depicted in Figure 2.1. Every antigen has a unique structure, and only those cells with receptors that fit the structure exactly will bind to that antigen. For this reason, the “fit” of the complementary structures of the antigen and the cell receptor is often compared to that of a lock and key. The foreign material usually has more than one antigen on its surface; as a result, several cells with different kinds of receptors may bind to the antigens on a single foreign particle and be stimulated to attack it.

Strictly speaking, a molecular structure is an antigen only if it can be recognized as foreign and stimulates an immune response. However, every person has molecular structures on the cells of his or her body that are capable of stimulating an immune response if they enter the body of another person who does not have the same antigens. For example, persons with type A blood have A antigens on the surface of their red blood cells. They can accept a blood transfusion from another person with A antigens, but blood from a person with B antigens will trigger an immune response which can be fatal. It is important that the body distinguish between “self” and “foreign” antigens. The body does not respond to its own or self antigens except in certain medical conditions in which some self antigens are mistakenly identified as foreign and stimulate an immune response. The result is an immune reaction against the self antigen which can lead to autoimmune diseases, such as rheumatoid arthritis.

After a receptor on the surface of a cell binds to an antigen on a foreign particle, the cell is activated and divides, forming B-cells and T-cells with receptors on their surfaces. The original cell is called a “progenitor” cell. Some of the clones produced from the T-cells remain at rest in reserve for the future. These “memory” cells are important because they can mount an enhanced

Figure 2.1
Specific immune response



response more quickly – in days instead of weeks – if the same antigen enters the body a second time. Their presence means that a person has been actively *immunized*. The other clones can differentiate, changing into more specialized cells. The change follows one of two paths, depending on the antigen and the particular cells involved. Each path leads to a different type of specific immune response.

One type is called a cell-mediated immune response. The end result is new cells of different kinds. “Killer cells” specifically react with the antigen on infected or foreign cells and destroy them. “Suppressor cells” suppress immune responses in order to regulate the process. “Helper cells” enhance other immune responses.

The other type of response is called an antibody-mediated immune response. In it, the end result is plasma cells that produce *antibodies*. Antibodies belong to a class of proteins, called immunoglobulins, that react specifically with the antigen that induced their production. The part of the antibody that reacts with the antigen has a structure that is almost identical to the receptor on the original or progenitor cell that recognized, bound to, and was stimulated to divide by the antigen. The antibodies bind to antigens on the surface of foreign material and work to destroy it in different ways. They can cause the foreign material to clump into larger particles that can then be recognized by non-specific defence cells and engulfed and destroyed by them. They can inactivate or neutralize foreign materials, including microorganisms and biologically active molecules, such as toxins. Alternatively, they can initiate further reactions that can lead to destruction of the foreign cells.

Immunity – the condition of being immune by having antibodies and cells that will react with a specific antigen – is the body’s most important means of protection against infectious disease. Immunity may result from infection, which stimulates the immune response and the production of memory cells. Alternatively, it may be created by deliberately exposing (for example, through injection, as in vaccination) a person to antigens that are the same as, or very closely related to, the antigens on the infectious microorganism. Because immunity takes some time to develop, persons in immediate danger of an infectious disease may be “passively” immunized by giving them preformed antibodies collected from immunized persons. The preformed antibodies are contained in a fraction of plasma often called gamma globulin. The preformed antibodies protect the recipient against the immediate threat but do not confer lasting immunity. This is because no memory cells have been formed and, once the injected antibodies are broken down, the person is no more resistant to infection than he or she was before the passive immunization. The presence of antibodies or immune cells to an infectious agent does not necessarily ensure that a person is completely protected from infection by the agent.

Components of blood

The body of an adult person contains approximately four to five litres of blood, which consists of liquid and cellular components. If whole blood is mixed with an agent that prevents it from clotting and is allowed to settle, it separates into three visible layers. The top layer, the plasma, is a yellow liquid and constitutes slightly more than half the volume. The bottom layer is red and contains the red blood cells. In between is a very thin layer, commonly called the "buffy coat," which contains the white blood cells and platelets. The main components of blood are depicted schematically in Figure 2.2.

Red blood cells (erythrocytes) carry oxygen to the tissues and are the most numerous of the cellular components. Each millilitre of blood contains approximately 5 billion red blood cells, all with the same size, function, and appearance. They are small and disc-shaped, with the centre slightly indented. Their shape enables them to travel through the tiniest capillaries and at the same time provides a large surface area for transferring oxygen. Red cells do not contain nuclei and therefore cannot divide and recreate themselves. They are the end products of cell divisions that begin in stem cells in the bone marrow. Normal red blood cells remain in circulation for about 120 days before they are removed and broken down in the liver or spleen. Their bright red colour comes from hemoglobin, the component that carries oxygen. Hemoglobin binds oxygen as the blood passes through the lungs and releases it throughout the rest of the body. The reactions involved in binding and releasing oxygen are complex, and even small chemical modifications of hemoglobin affect them.

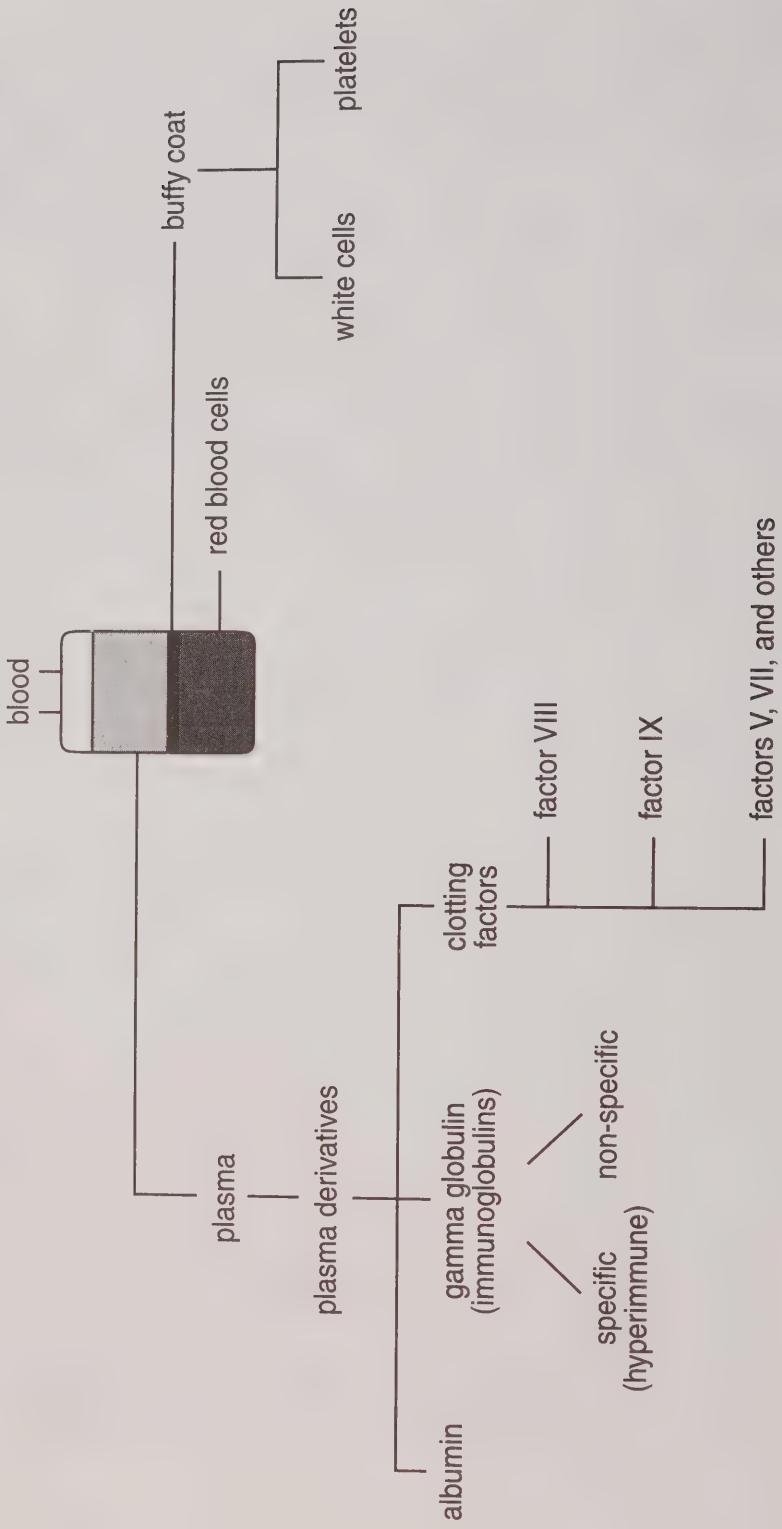
White blood cells (leucocytes) are responsible for clearing the blood of debris and combatting infection. There are many different types, with life spans that vary from hours to years. All white blood cells have nuclei and are also derived from stem cells in the bone marrow. Functionally they are divided into three groups – granulocytes, monocytes, and lymphocytes.

Granulocytes are divided into three types. The most abundant, neutrophils, are important in non-specific immunity and help clear the body of foreign material by engulfing and digesting small particles, including microorganisms. Basophils, the least abundant, play an important role in the release of histamine, the chemical that causes allergic reactions and increases local blood flow in response to injury. Eosinophils are important in the body's reactions to parasites.

Monocytes are large and can leave the circulatory system and enter tissues, where they engulf and destroy microorganisms and other foreign material. They play an important role in processing antigens to a form that is effective in stimulating an immune response.

Lymphocytes are usually small and regularly shaped; in each, the nucleus occupies most of the cell. They are important for the body's specific immune response to foreign material. They include B-cells, also called B-lymphocytes,

Figure 2.2
Blood components and products



which are derived from and mature in the bone marrow, and T-cells, also called T-lymphocytes, which, although initially derived from the same stem cells in the bone marrow, are called “thymus-derived” because they mature in the thymus. B-cells are essential for antibody-mediated immune responses; they can develop into plasma cells, which are responsible for producing antibodies, or they can become memory cells and stimulate an increased antibody response to a foreign antigen to which the body has previously reacted. T-cells may attack foreign invaders directly. They include further subtypes, such as helper cells (which have a certain type of antigen called CD4 on their surface and are often called CD4 T-lymphocytes or CD4 T-cells), suppressor cells, and killer cells (which have antigens called CD8 on their surface and are called CD8 T-lymphocytes). T-cells are important for both cell-mediated and some antibody-mediated immune responses.

Platelets are fragments of large bone marrow cells. They do not have nuclei and are very short-lived. They are essential for starting the coagulation process. When a blood vessel is damaged, it constricts. Platelets adhere to the damaged cellular lining and then to one another, forming a temporary plug. This process stimulates the rest of the coagulation process, which involves many protein factors present in the plasma.

Plasma is the fluid in which the blood cells are suspended. It is composed mostly of water, but also contains many proteins, salts, lipids, and a variety of nutrients and products of metabolism. The proteins have a variety of functions, individually and collectively. If the concentration of protein falls below a certain level, fluid will leak from blood vessels into the surrounding tissue, and both blood volume and blood pressure will fall. Albumin, the most abundant protein in plasma, is the most important in maintaining blood volume and pressure.

The proteins contained in plasma include *coagulation* or *clotting factors*. These factors are activated when a blood vessel wall is damaged and platelets begin adhering at the break. The coagulation system involves a cascade of reactions, each protein (or factor) triggering a reaction from the next in the sequence. The net result of the chain reaction is conversion of fibrinogen, also a protein in plasma, to fibrin, the “cement” that solidifies the platelet plug to form a clot. Deficiency of any of the factors increases the chances of uncontrolled bleeding and the need for treatment with blood or blood products. The factors are identified by Roman numerals according to the order of their discovery, not their position in the sequence. The factors that are most important in transfusion medicine are VIII and IX, because deficiency in either of these factors leads to bleeding disorders called hemophilia. Factor VIII circulates in the plasma in combination with another protein called the von Willebrand factor. The von Willebrand factor is needed for factor VIII to function, so a deficiency in it also leads to increased bleeding and the need for blood and blood products. More will be said about hemophilia and clotting factors later in this chapter.

Just as deficiencies in any of the factors or components in the coagulation system can lead to life-threatening conditions, overactivity or lack of control of the system can have serious consequences. Proteins in the plasma, such as anti-thrombin III, are responsible for regulating coagulation by ending the chain reaction. A deficiency in the regulators may cause the coagulation process to become overactive, leading to thrombi, or blood clots, which can block vessels and lead to death.

Plasma also contains *immunoglobulins* and other proteins important in the body's immune responses to foreign material. Immunoglobulins include the antibodies that help to fight specific infections. Different classes of immunoglobulins serve different purposes. For example, immunoglobulin E (IgE) is responsible for the immediate hypersensitivity reactions that, through the release of histamine, cause certain allergic and anaphylactic reactions which, in persons with extreme sensitivity, can be fatal. Immunoglobulins M and G (IgM and IgG), the most common, help to protect the body from bacteria and other molecules, particles, and cells recognized as foreign. They go into action, for example, when bacteria enter a cut and it becomes infected.

Immunoglobulins can be derived from blood and used to treat certain conditions. Most of us have antibodies to a wide variety of antigens. If the protein fraction called gamma globulin, which contains immunoglobulins, is separated from blood, the result is a non-specific immune globulin preparation. This kind of preparation is currently used to treat persons with immune deficiencies that are caused by a genetic defect or that occur as side-effects of disease or treatment. Non-specific immune globulin preparations are often given, for example, to patients who receive transplanted organs or tissues. A patient undergoing this kind of surgery normally is given drugs (immunosuppressants) to decrease the body's immune response, so the patient's body does not recognize the transplant as foreign and reject it. But drugs that suppress the immune response also make a patient more susceptible to infection. The non-specific immune globulin preparations provide some protection.

Some blood has a high concentration of antibodies to a particular antigen because the person has been immunized or recently infected. In that case, the immunoglobulin fraction derived from it may be further purified to provide a specific immune globulin preparation. Specific immune globulins are used to provide temporary protection for persons thought to have recently been infected with a particular disease agent. For example, tetanus immune globulin is given to persons suspected of having been exposed to tetanus.

An understanding of immunoglobulins is important in transfusion medicine. The patient receiving the transfusion may have antibodies that will react with and destroy or inactivate the foreign cells (such as red or white blood cells), platelets, or molecules (such as coagulation factors) in the transfused blood. The most acute type of reaction occurs when the transfused

blood has come from a donor with an incompatible blood type. In this reaction, IgG or IgM antibodies in the recipient's blood recognize antigens on the surface of the transfused red cells and attach to them. This process can stimulate a cascade of reactions involving almost a dozen other proteins in the plasma. The reaction destroys the transfused red cells. In addition, the massive release of hemoglobin from the destroyed red cells is toxic for the kidneys and can prove fatal.

Processing blood to components and plasma products

In Canada, blood is collected from volunteer donors at permanent or temporary collection sites. The process starts when a donor arrives at a clinic and registers. A staff member checks the person's identity and examines records to see whether there has been any reason to refuse a donation in the past. The donor's hemoglobin level is measured. He or she is then given pamphlets that include information about who should not donate. The person is asked to complete a written questionnaire designed to identify behaviours, exposures, treatments, family history, and travel that could put a person at increased risk of coming into contact with and thereby carrying and transmitting diseases. A nurse confirms that the donor has read the pamphlets, and asks the donor questions to determine whether the person is at increased risk for diseases. If an answer to one of the questions points to a potential problem, the nurse can refer to a manual to determine, for example, whether a person on medication or reporting a history of certain conditions or exposures should be deferred and, if so, for how long. The nurse also conducts a visual inspection of the donor's arms for evidence of drug abuse, and checks temperature and blood pressure. The donor is asked to fill out a confidential unit exclusion form (a means by which those who recognize that they are at high risk of contracting AIDS, but find themselves in a situation where they cannot avoid giving blood, can say privately that their blood should not be used for transfusion). The nurse gives him or her a set of labels bearing a bar code unique for that visit. Before blood is taken, there is a further identity check. The donor's skin is scrubbed twice with an iodine solution to remove surface bacteria which could enter the needle when it pierces the skin. The actual collection ends when 455 millilitres of blood have flowed into a bag containing an anticoagulant solution. During collection, the bag and a series of tubes and adjoining bags, all of them forming one sterile closed system, are individually labelled with the bar code, and a label with the same bar code is attached to the donor's record. The blood bags are sent for processing, and the samples in the tubes are sent to a laboratory for testing.

In the processing, the blood bags are spun in a centrifuge to separate the blood into two or three components, all within the closed system of adjoining bags. The yellowish plasma is separated into one bag. The buffy coat

containing the white cells and platelets may also be separated, depending on the current need for platelets. The red cells are mixed with a nutrient solution from one of the adjoining bags to help keep them healthy during storage. The components in their individual bags are detached and stored in quarantine until the test results have been interpreted. Red cells are kept at refrigeration temperature (between 2°C and 4°C), and platelets at room temperature; units of plasma are either refrigerated or frozen as soon as possible, depending on how the plasma is to be used.

The samples are tested in a laboratory to determine the blood type (A, B, AB, or O, and Rh-positive or -negative) and to detect unusual antibodies in the plasma. These results must be accurately recorded because a mismatch between the blood of a donor and that of a recipient can lead, as has been explained, to severe, possibly fatal, transfusion reactions. Samples of the blood are also tested for markers of certain infectious diseases. Some of the tests used in Canada identify the presence of an antigen on a disease-causing organism, such as a surface antigen on the hepatitis B virus (in which case the antigen is the marker). Other tests identify the presence of antibodies to the disease agent (in which case the antibody is the marker). The presence of antibodies to the human immunodeficiency virus (HIV), hepatitis C virus, and human T-cell lymphotropic viruses I and II (HTLV-I and II) indicate (mark) the presence of those viruses. Donations are also tested for the presence of the spirochete bacterium that causes syphilis. If the tests detect none of these infectious disease markers, the donated unit is labelled and stored, ready for distribution to hospitals. If a sample tests positive, the donation is removed and destroyed and samples are sent to a central laboratory to confirm the initial test result.

The confirmatory tests at the central laboratory usually involve a totally different, often more complex, method that is more specific for detecting infectious disease markers. The initial screening tests are very sensitive; that is, almost every sample that contains the infectious disease agent will test positive. However, they are not very specific; as a result, many of the samples they identify as positive do not, in fact, contain the infectious disease agent. It is therefore important to check the initial results to find out whether the blood does indeed contain the infectious disease agent. In Canada, all donors whose blood tests positive in the initial screening tests are told of the result and asked not to donate blood in the future. The results of positive confirmatory tests are communicated to the donor, usually through his or her physician, so that the donor may be told and offered appropriate treatment and counselling.

During the screening, collection, processing, and testing of blood, several checks are made to ensure that records and results agree. Record keeping throughout the process, from donor information through test results to distribution of units, is gradually being computerized to reduce the chance of error.

Donations of whole blood cannot meet the total demand for platelets or for the several specialized products derived from plasma, collectively called plasma derivatives or blood products. To fill this gap, plasma and platelets alone, without red blood cells, are collected using a process called *apheresis*. The process is similar to that used in collecting whole blood except that the blood does not simply flow into a bag. Instead it is passed through a closed, sterile system in a machine that separates the various components and returns the red blood cells to the donor. The collection takes longer because the equivalent of four to six units of blood, instead of only one, is processed at each donation. Donors can undergo apheresis more frequently than they can donate whole blood because the normal human body can replace lost plasma and platelets much more quickly than it can replace lost red blood cells. Apheresis donors are given more comprehensive health examinations than regular donors, and the concentration of protein in their plasma is measured to ensure that they are not being harmed by the process.

The additional supply of platelets from apheresis is needed because platelets have a short shelf life – only three to five days – and the yield of them from whole blood donations is low. According to many experts, platelets derived from whole blood have very little activity after being stored for several days. There are further reasons for collecting platelets through apheresis, however. It normally takes four or five donations of whole blood to produce the number of platelets required for a single infusion of platelets. To obtain this number it is necessary to pool platelets from several whole blood donations. The process of pooling platelets creates several additional risks for the recipient. First, during pooling the closed sterile system of bags must be broken, and contamination may result. Second, platelets have tissue antigens on their surface that are not present on red blood cells and are not tested for when blood groups are determined; there is a risk, therefore, that the recipient's immune system will recognize the infused platelets as foreign and will form antibodies to them, and increasing the number of donors increases that risk. The antibodies thus formed remain in the recipient, and when he or she receives another transfusion they could react to the infused platelets and render them ineffective. Through apheresis, the number of platelets required for one infusion can be supplied through a single donation. When a patient has a chronic medical condition that requires many infusions of platelets, an arrangement is often made to find one, or sometimes more than one, donor who has a reasonably good antigenic match with the patient. Whenever the patient needs an infusion, that donor is asked to undergo apheresis. This arrangement reduces the likelihood that the patient will form antibodies to the platelets.

Apheresis is also required to meet the demand for blood products derived from plasma. The plasma that is collected from apheresis is called "source plasma"; the plasma separated from whole blood donations is called

"recovered plasma." Some plasma is distributed to hospitals, but most is frozen, to be further processed into specialized products by a process called *fractionation*. Canada has no means of processing plasma on a large scale and, as a result, Canadian plasma is stored and shipped to the United States for fractionation.

The basic process for fractionating plasma was developed in the 1940s by Dr Edwin Cohn at Harvard University. He added increasing concentrations of alcohol to the plasma while altering its acidity in order to precipitate different proteins. These proteins were then separated by centrifugation. His method is still the basis of the processes used by most manufacturers for large-scale fractionation, although a variety of modifications have been made to simplify the isolation of the clinically important fractions and to improve yields. Procedures have also been added to purify the crude products and to inactivate viruses that may be in the plasma.

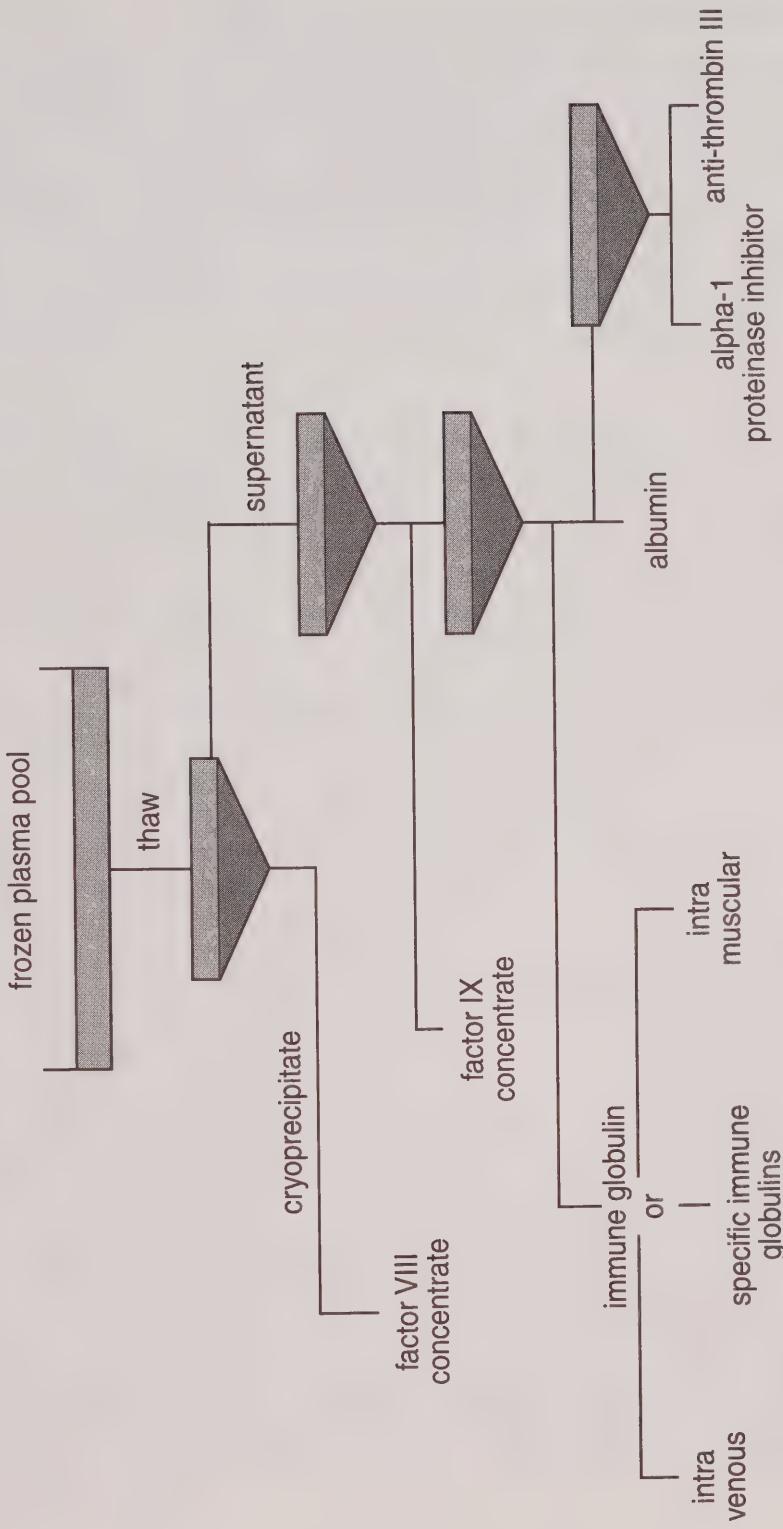
Large-scale fractionation involves pooling plasma from at least 1,000 donors and from as many as 60,000 donors when recovered plasma is used. The number is considered optimal for achieving economies of scale and also to ensure a wide spectrum of antibodies in preparing non-specific immunoglobulin.

The pooled plasma is thawed and may be tested for the presence of genetic material from certain viruses. The tests used are more complex and more sensitive than those used to screen the initial donations.

A portion of the plasma does not dissolve when thawed; this *cryoprecipitate* is removed and becomes the starting material for production of factor VIII concentrate. The cryoprecipitate also contains fibrinogen, von Willebrand factor, and factor XIII, and before more sophisticated methods of processing were developed cryoprecipitate was used to treat patients with deficiencies in these coagulation factors. Today, the cryoprecipitate is processed to separate its various components for more effective use. The liquid remaining after the cryoprecipitate is removed is fractionated, using the same basic process developed by Dr Cohn, into other specialized products. One of these is albumin. Others are gamma globulin, factor IX concentrate, alpha-1 proteinase inhibitors (used to treat persons with deficiencies that affect the functioning of the lungs), and anti-thrombin III (used to treat persons with certain clotting disorders). Figure 2.3 is an illustration of the fractionation process.

Coagulation factors are now commonly freeze-dried during processing and are packed in glass vials. They are dissolved in sterile water for use, and the solution is injected into the patient. Because the factors are purified and highly concentrated during processing, the solution contains many times the amount of factor that would be contained in the same volume of plasma.

Figure 2.3
Plasma fractionation by cold ethanol precipitation and purification



Transfusions of blood or blood products

The use of whole blood for transfusions has become very rare. Since the advent of plastic bags and efficient separation techniques, only the components that are needed are normally transfused. It is still common, however, to refer to transfusions of red blood cells as blood transfusions or transfusions of blood.

The major indications for transfusing blood components or blood products are: (1) acute blood loss, (2) diseases and treatments that affect the ability of the body to produce blood, (3) defects in the coagulation system, and (4) immunologic reactions and deficiencies. Transfusions of white blood cells are rare.

Acute blood loss

The original reason for blood transfusions was to replace blood lost through excessive bleeding. Excessive bleeding may occur as a result of major surgery, trauma, or massive internal bleeding. In acute blood loss, the blood pressure falls; as a result, the heart may not get enough blood to the vital tissues to provide sufficient oxygen to sustain cell function. The need for treatment may be urgent. Further blood loss needs to be prevented and lost functions restored, particularly circulation and oxygen-carrying capacity. Platelets too may have to be replaced because they are also lost in the bleeding and consumed in the body's efforts to stop the bleeding. If the bleeding can be stopped quickly and the patient's condition stabilized, transfusion may be unnecessary. The body is able to compensate for the loss of large amounts of blood if circulation to vital organs is maintained and the demands on the tissues are minimized.

Because the critical function of blood is delivery of oxygen to tissues, the decision whether or not to transfuse used to be based primarily on hemoglobin level. A hemoglobin concentration of 100 grams per litre was considered to be the "transfusion trigger," below which transfusions of red blood cells were considered necessary. It now is recognized that many other factors need to be taken into consideration, especially the efficiency of the patient's heart.

Several techniques have become available for preventing blood loss, for stimulating the body's ability to produce more red cells, and for recycling the patient's own blood in surgery. In cases of acute loss, however, the need for treatment may be immediate; today, the only alternative to blood transfusion is fluid replacement or a volume expander to maintain the level of fluid in the circulatory system. Albumin, for example, is transfused as a volume expander in cases of traumatic blood loss and in the treatment of burns when excessive fluid has been lost. Volume expanders that are not derived from blood can also be used in emergencies; these substances include starches, salt, and protein solutions. Replacement of oxygen-carrying capacity with anything other than red blood cells is, for the most part, still in the experimental stage.

Diseases and treatments that affect the ability of the body to produce blood

Some diseases – for example, aplastic anemia – decrease the bone marrow's ability to produce blood cells. In such cases, the only treatment currently available, other than blood transfusion, is to transplant bone marrow. Other diseases indirectly affect the body's ability to produce blood cells. Leukemia is uncontrolled, malignant growth of white cells leading to anemia (deficiency in red cells) or thrombocytopenia (deficiency of platelets) or both. Leukemia, like other cancers, is usually treated with agents that kill the rapidly dividing cells, but these agents also damage the cells that replenish the normal blood cells. Both leukemia and the conditions caused by its therapy are often treated with transfusions of red cells, platelets, or both.

Some genetic defects can cause defective hemoglobin, as in sickle cell anemia and thalassemia. Transfusions are often used in treating these diseases, both to increase the oxygen-carrying capacity of the patient's circulatory system and to suppress the patient's production of the red blood cells containing defective hemoglobin. In sickle cell anemia, because of the defective hemoglobin, the patient's red blood cells are distorted in shape, with the result that they tend to block capillaries; they thus prevent oxygen from reaching the tissues and lead to tissue death and considerable pain. In thalassemia, the body's attempt to increase the bone marrow's production of red blood cells causes abnormal bone marrow function, which in turn affects bone development.

Anemia frequently occurs in cancer patients and can be caused by chemotherapy, radiation therapy, or tumour infiltration of the bone marrow. A tumour may also cause malnutrition or abnormal iron metabolism that can lead to anemia. Large, solid tumours have a high demand for oxygen and nutrients and thus can deplete the supply to the rest of the body. To provide the increased nutrients and oxygen needed to meet this demand, new blood vessels are formed and there is an increased blood flow to the area of the tumour. If the tumour is surgically removed, there is likely to be a significant blood loss, commonly treated with a blood transfusion. In Canada cancer and its treatment are responsible for a significant proportion of the demand for blood transfusions and infusions of blood products.

Anemia associated with chronic kidney failure is also treated by transfusion. The anemia occurs, in part, because the impairment of kidney function leads to a deficiency in erythropoietin, a growth factor that stimulates red blood cell production. Recently erythropoietin has been synthesized, and it is now used as an alternative to blood transfusion for certain types of anemia and to boost red blood cell production in persons who want to deposit blood for their own, imminent surgery.

Anemia can also be caused by a lack, or ineffective absorption, of iron. Other conditions, either natural or drug-induced, can often cause red cells to be destroyed more rapidly than usual. Transfusions are normally not used in treating these conditions.

Platelets may be transfused to treat patients who have lost platelets from excessive bleeding, or who are not producing enough platelets on their own because of leukemia or other diseases and treatments that suppress the production of blood cells.

Defects in the coagulation system

Deficiencies in the coagulation system may be inherited or acquired. Persons with such disorders are subject to uncontrolled bleeding and may need frequent transfusions. Several types of genetic defects can affect the production or function of one of the coagulation factors. The most serious deficiencies occur in factor VIII and factor IX and lead to the conditions collectively called hemophilia. In Canada, approximately 2,500 persons suffer from hemophilia and many thousands of other persons suffer from a deficiency in one of the other factors, most commonly von Willebrand factor. Conditions that are acquired, as in patients with severe liver failure, usually involve a deficiency in several factors or components or both.

Hemophilia A, the most common form of hemophilia, is a genetic disorder transmitted by females and manifested almost entirely in males. This is called a sex-linked disorder because the gene coding for factor VIII is present on the X chromosome. Because males have only one X chromosome, any defect or mutation in that gene will decrease the production of functional factor VIII. Although it is not impossible, it is very rare for a female to have defective genes on both X chromosomes and to exhibit clinical symptoms of hemophilia. Approximately 30 per cent of hemophilia A cases are not inherited but are thought to result from spontaneous mutations in the gene coding for factor VIII. This non-inherited form of hemophilia A also primarily affects males. The clinical severity of hemophilia A depends on the amount of functional factor VIII the patient can produce. In the blood of mild hemophiliacs, the level of functional factor VIII is between 6 and 30 per cent of that present in normal persons; in moderate hemophiliacs, between 1 and 5 per cent; and in severe hemophiliacs, less than 1 per cent.

Von Willebrand's disease, another genetic disorder, affects both sexes and involves a deficiency of von Willebrand factor. Because von Willebrand factor is important for carrying and protecting factor VIII and for stimulating its production, a deficiency leads to a decrease in the production of factor VIII and less activity in the factor VIII that is present.

Approximately 14 per cent of hemophiliacs have hemophilia B, or Christmas disease, a deficiency in factor IX. This is also a sex-linked genetic defect primarily affecting males.

Those hemophiliacs who are most seriously affected have frequent bleeding episodes, often more than once a week. Without treatment, recurrent bleeding into their joints and muscles results in painful and disabling deformities. Bleeding into the brain and other internal organs can be fatal. Until the 1950s,

severe hemophiliacs had a significantly shortened life expectancy, and most were severely disabled as a result of recurrent bleeding into joints.

The treatment for hemophilia used only to be reactive – that is, by attempts to stop uncontrolled bleeding and replace lost blood through transfusion. For severe hemophiliacs, this treatment involved repeated and extensive administration of blood, and later of plasma, in an attempt to provide enough coagulation factors to control bleeding. Understanding of coagulation factors and of the forms of hemophilia has increased, and techniques for recognizing and separating the different proteins or protein fractions have improved. Beginning in 1964, new treatments were developed to prevent or reduce uncontrolled bleeding, including internal bleeding. Initially, persons with hemophilia A and von Willebrand's disease were given infusions of cryoprecipitate, which has a higher concentration of clotting factors and therefore did not need to be administered as frequently. More recently, both hemophilia A and B have been treated with purified factor concentrates manufactured from pooled plasma, or with clotting factors synthesized in the laboratory using recombinant biotechnological techniques that do not require plasma as the starting material. These newer treatments can be administered at home, either by the patient himself or by a parent or other caregiver.

A chemical, desmopressin (DDAVP), can be used for some hemophiliacs to increase the level of circulating factor VIII. It is thought to stimulate the release of factor VIII and von Willebrand factor from sites in the body where they are produced and stored. For DDAVP to be effective, however, some normal factor VIII must be present. DDAVP has been found to be particularly useful in treating persons with mild hemophilia A and mild to moderate von Willebrand's disease.

Acquired bleeding disorders occur temporarily in some patients who have received transfusions of stored blood, because the coagulation factors and platelets that control bleeding are unstable and can deteriorate during storage. Acquired bleeding disorders can also occur in patients who have severe liver failure, because the coagulation factors are produced in the liver. Persons using anticoagulants may also experience uncontrolled bleeding. These patients may require infusions of fresh plasma, cryoprecipitate, or platelets.

Overactivity of the coagulation process can be as serious as deficiency in coagulation factors. It can lead to the formation of unwanted clots (thrombi), which can cause vital organs to fail. When this happens, treatments can be given by using anticoagulants to prevent clotting, thrombolytic agents to break down clots, or blood products to decrease the formation of the clots. For example, some persons have a congenital deficiency of anti-thrombin III, a molecule that helps to regulate the clotting process. Anti-thrombin III can be isolated from plasma and used to treat persons who are deficient in it to prevent the formation of clots. It can also be used as a preventive measure for deep vein thrombosis in persons undergoing hip and knee surgery. In rare

cases, coagulation factors are used to treat disseminated intravascular coagulation, a condition involving widespread activation of clotting factors. Disseminated intravascular coagulation can occur during pregnancy or when certain chemicals are released from red blood cells. The widespread activation depletes the plasma of clotting factors and, as a result, any bleeding that occurs may be uncontrolled.

Immunologic reactions and deficiencies

Immunoglobulins may be used to treat a variety of conditions involving deficiencies in immune response that are caused by genetic defects or that result from disease or treatment. Examples have been given in the preceding discussion of immunoglobulins.

Blood products may also be used to treat unusual immune reactions, including idiopathic thrombocytopenia purpura, a disease caused by an immune destruction of platelets. It can be acute or chronic in children or adults and is often associated with AIDS. For reasons that are unclear, treatment with antibodies specific to the Rh antigen has been shown to increase the number of platelets in these patients.

Another unusual immune reaction occurs in approximately 10 per cent of persons with hemophilia A who form antibodies to the purified or synthetic factor VIII preparations used to treat them. The antibodies, commonly called inhibitors, decrease the effectiveness of the factor VIII these patients receive. To help prevent uncontrolled bleeding, other treatments are sometimes required, such as clotting factor complexes or factor VIII derived from the plasma of pigs, which has a different antigenic structure.

A third example of unusual immune reactions is hemolytic disease of the newborn. This potentially fatal condition may occur when a woman who is Rh-negative (that is, a woman without the Rh antigen on the surface of her red blood cells), and who has antibodies to the Rh antigens, carries a fetus that is Rh-positive. The mother may have developed the antibody in one of two ways. She may have been immunized by receiving Rh-positive blood in a transfusion, or she may have carried a previous fetus whose Rh-positive blood entered her circulatory system during birth or an obstetrical procedure. The risk is that the mother's Rh antibodies can cross the placental barrier to the Rh-positive fetus and destroy its red blood cells. The infant may be mildly or severely affected. Severely affected babies are given an exchange transfusion of blood at birth, both to ensure that the baby has adequate oxygen-carrying capacity and to remove antibodies that crossed from the mother. The preferred treatment is, however, preventive, treating the cause rather than the symptoms. Rh-negative women who have not yet developed Rh antibodies are given specific Rh antibody to prevent them from forming their own when they encounter Rh-positive blood. These infusions are given just before birth, before amniocentesis, or during any other procedure that might damage the placenta and allow fetal cells to enter the mother's

circulatory system. As an additional measure against the development of Rh antibodies, experts advise against giving Rh-positive blood to any Rh-negative woman of child-bearing age except in an emergency.

White blood cells

Transfusions of white cells are considered to be of doubtful benefit. Granulocytes are the only white cells that are transfused, and they are used only to treat infected newborn children and persons with severe chronic infections that do not respond to antibiotics. Transfusions of this kind are rare because granulocytes are difficult to collect in a usable form and are short-lived.

Risks in transfusion

Transfusions of blood components and infusions of blood products are not without risk. A variety of unfavourable reactions may occur. Broadly speaking, they can be grouped into immune and non-immune reactions.

Immune reactions

These reactions are caused by inherent differences between the antigenic structures of the blood of a donor and that of a recipient. The strength and seriousness of the reaction depend on a number of factors, such as the strength and prevalence of the antigens that are different, the presence of antibodies, any previous exposure of the recipient to the foreign antigens, and the state of the recipient's immune system.

In most immune reactions, the recipient's body reacts against the donation. The most severe reaction of this kind is intravascular hemolysis, which occurs when a patient receives blood incompatible with his or her own blood type – A, B, AB, or O. The antigens on the surface of red blood cells that determine which ABO blood group we belong to are the strongest and most prevalent. We all have natural antibodies to the A or B antigens not present on our own red blood cells. Therefore, if we receive transfused blood that has antigens we do not have, our antibodies react with the transfused red cells and destroy them. The process releases free hemoglobin and other chemicals, including those responsible for stimulating the clotting sequence, leading to disseminated intravascular coagulation. The reaction can be fatal. The frequency of fatal hemolytic transfusion reactions is estimated to be in the range of one per 100,000 units transfused to one per 1 million. The reaction is usually caused by the transfusion of mislabelled blood, by mistakes in testing, or by errors in the choice of the blood to be transfused at the hospital, mistakes colloquially known as "hanging the wrong bag."

Antigens other than those of the ABO system, including the Rh antigen, are also present on the surface of red blood cells. Antibodies to them do not occur naturally, and are likely to be present only if a person has been previously exposed to the antigen through pregnancy or previous transfusions. It is possible to test for the presence of these antibodies, but they may be

undetectable until the recipient is again exposed. When that happens, antibodies will be produced rapidly and can cause delayed transfusion reactions. These reactions are rarely fatal.

White cells carry antigenic markers common to most tissue cells, which are not present on red blood cells. White cells in transfusions induce recipients to produce antibodies to those antigens. The white cells are usually cleared from circulation before the antibodies, if formed, can react with them. If, however, a patient receives additional transfusions or an organ transplant containing the antigens already recognized as foreign, the antibodies will already be formed and will react with white cells in the transfused or transplanted cells and cause serious reactions.

Other immune transfusion reactions can result from antigens present on platelets or plasma components. The most serious occur in recipients who lack one particular class of immunoglobulins, IgA. If a recipient with this deficiency produces anti-IgA antibodies in response to IgA in the transfused blood, the result can be a severe allergic reaction (an anaphylactic reaction) that is potentially fatal. A less serious immune transfusion reaction is post-transfusion purpura (red or purple blotches on the skin indicating small hemorrhages), caused by antibodies in the recipient that cause destruction of transfused platelets.

The most common and least serious immune transfusion reactions are febrile reactions (that is, reactions that induce a fever) and allergic reactions that result in urticaria (hive-like spots on the skin). White cells, when stimulated or as they age, may release cytokines (proteins that are important for stimulating other cells) that are thought to cause many of the febrile transfusion reactions. Other febrile reactions are less severe forms of the reactions already described. The mechanism of some of the allergic reactions is not completely understood, but the reactions are thought to result from antibodies reacting with plasma components.

In other types of immune transfusion reactions, the donated blood reacts against the recipient. One example is transfusion-related acute lung injury, a rare but life-threatening complication thought to have an immunological basis. Another is graft-versus-host disease. This condition occurs when lymphocytes from the donor that are immunocompetent (that is, capable of mounting an immune response) are not recognized as foreign by the recipient and are allowed to colonize the bone marrow. These invading cells identify the recipient as foreign and begin an immune attack against the recipient's cells. The result can be fatal. Persons whose immune systems are suppressed are particularly at risk of graft-versus-host disease because their own cells are less likely to recognize and attack the donor cells. Persons with normally active immune systems are also at risk of graft-versus-host disease, especially when receiving blood from a close relative, especially a parent.

The risk of graft-versus-host can be almost completely eliminated by irradiating the blood components to be transfused, thus inactivating the lymphocytes without destroying the functional capacity of the red blood cells and platelets. Many other immune transfusion reactions can also be avoided or prevented by removing white cells from the blood being transfused. The number of white cells can be significantly reduced by passing the blood through specialized filters, either during processing or at the bedside before transfusion. The process of decreasing the number of white cells in units of red blood cells to be used for transfusion is called leucocyte depletion or leucocyte reduction.

There is increasing evidence that transfusion of allogenic blood (that is, blood from another person) tends to suppress the recipient's immune system. The mechanism and clinical significance are not yet fully understood. It is also unclear whether the immunosuppressive effect is the cause of enhanced tumour growth that has been observed in some studies.

This discussion of immune transfusion reactions has, for the most part, not distinguished between red blood cells and other blood components. Component separation is never complete. For example, red blood cell concentrates contain some white cells, and units of platelets contain some red blood cells. Therefore, although platelets do not have A or B antigens, reactions can occur if transfused platelets have come from donors who are not ABO-compatible with the recipient.

Non-immune reactions

These reactions can result from contamination of the blood by bacteria or chemicals during collection, processing, storage, or administration. This type of contamination can usually be prevented by meticulous handling. Even with great care, however, adverse reactions are possible. For example, a recipient with liver damage may suffer a reaction because his or her liver cannot clear the citrate that was used as an anticoagulant in the transfused blood components.

Bacterial contamination can come from a variety of sources. Bacteria may be temporarily present in large numbers in a donor's circulatory system as a result, for example, of the extraction of a tooth or because of an acute infection; they may be on a donor's skin where the needle is inserted for collection; or they may enter the donated blood during processing. This sort of contamination does not always cause a transfusion reaction. Depending on the type of bacteria and the general health of the recipient, small numbers of bacteria can often be cleared by the recipient's immune system. Generally, for a transfusion reaction to occur the bacteria must have been able to survive and multiply during storage. Very few bacteria can multiply in the low temperatures at which red blood cells and plasma are stored, and some, such as the spirochete that causes syphilis, cannot survive for more than a few hours. However,

some bacteria are capable of multiplying even at temperatures as low as 4°C, and one in particular, *Yersinia enterocolitica*, has been known to cause fatal reactions in patients who received contaminated red blood cells that had been stored. Platelets are inactivated if they are refrigerated, and are therefore stored at room temperature, which is more conducive to the multiplication of bacteria. As a result, contamination of platelets is more likely to lead to clinically significant reactions, including death, than contamination of other components.

The greatest risk of contamination, and the most difficult to control, is from infectious disease agents present in the donor's blood at the time of donation. Many disease-causing agents can enter the bloodstream, and most will be cleared by the body's natural defences without causing disease. Some commonly carried in blood do not pose a risk to healthy persons but can cause life-threatening infections in persons whose immune systems have been suppressed, either through disease or treatment. Other organisms appear to cause clinical disease in every person who is exposed.

Of great importance is the fact that some organisms can remain in the bloodstream for extended periods before, or after, the manifestation of disease. A person thus may carry and transmit a disease-causing agent without having clinical signs or symptoms and, in some cases, without the disease-causing agent being detectable. A person who carries and can transmit a disease-causing agent, but does not have clinical signs or symptoms, is called a carrier. It is carriers who pose the greatest risk to the safety of the blood supply, especially if they donate during the "window period" – that is, the time when the agent is not detectable – or if no test is performed.

Plasma derivatives

Infusions of plasma derivatives may also cause adverse reactions, although immune reactions from infusions of these blood products are less likely to be serious. Plasma derivatives do not have the same degree of antigenic diversity as the cellular components of blood. Albumin from one person, for example, is antigenically the same as albumin from any other. Immune reactions to plasma derivatives are unlikely to pose a risk unless the recipient has always lacked a particular plasma protein, such as, in the example given previously, IgA. Plasma derivatives may or may not be highly purified. Their safety and antigenic status can be affected by the physical and chemical treatments they undergo in processing and the amount and nature of other proteins that remain after the preparation has been purified. The risk of bacterial and viral contamination of plasma is the same as for other blood components, but, because proteins are smaller and more resistant to physical and chemical treatment than blood components, plasma derivatives can be filtered, heated, or treated with chemicals to remove or kill many of the contaminating microorganisms. Some blood products, for example, undergo vigorous treatment to inactivate viruses; however, the treatment may alter the

antigenic structure of the active ingredient. A number of factors determine whether plasma derivatives will cause adverse reactions in the recipient. They include the purity and efficacy of the product, possible contamination of the plasma, the efficacy of viral inactivation treatments, side-effects caused by the formulation (the medium in which the product is dissolved after fractionation and purification), and new antigens formed during processing.

HIV and hepatitis C

A number of organisms that pose a risk to the blood supply were described in the Interim Report. The two most important for the safety of the blood and blood products in the 1980s were the human immunodeficiency virus (HIV) and the hepatitis C virus. What follows is a brief description of these two viruses and the conditions caused by infection as they are understood in 1997. This understanding represents the accumulation of knowledge from many research and clinical studies during the 1980s and early 1990s. The principal concern of this Report relates to the events surrounding the contamination of the blood supply in the 1980s. It is therefore essential to emphasize that our knowledge of these two organisms was and is still evolving. The information available at the time of specific events and decisions is described in more detail in the discussion of these events.

Acquired immunodeficiency syndrome (AIDS) and human immunodeficiency virus (HIV)

In medical science, the usual sequence of events in a "discovery" is that a disease is described, its pathogenicity (the cellular events, reactions, and mechanisms occurring in the development of the disease) is investigated, and specific "causes," in some cases microorganisms, are "discovered." In some diseases, the causative microorganisms are new to science; in some, they are known for some other reason; and in others, the disease is well known but has been thought to be caused by something else.

AIDS was considered a new disease, or, more specifically, a syndrome – a number of signs or conditions that occur together. Our description and our understanding of it are still evolving for two reasons: first, our understanding of the destruction of the immune system and the diseases that ensue is increasing; and, second, new therapies are altering the course and manifestations of the disease and causing changes in the disease-causing agent.

Because AIDS has many manifestations, it is not known when it first occurred. In the late 1970s, however, physicians became aware of an increased incidence of some rare infections and forms of cancer, and of patients suffering from several and severe bouts of infections that in healthy persons do not cause serious effects. Gradually they came to recognize that there was probably something destroying the immune system, leaving persons affected vulnerable to many diseases that eventually proved fatal.

What is now accepted by the overwhelming majority of medical scientists as the cause of AIDS was first identified several years after the syndrome was described. It was “discovered” in 1983 and 1984 by several scientists and named, variously, lymphadenopathy-associated virus (LAV), human T-cell lymphotropic virus III (HTLV-III), and AIDS-related virus (ARV), and eventually, by common agreement, human immunodeficiency virus (HIV). There are still at least a few scientists who do not believe that HIV causes AIDS.

Since it was first described, there have been thousands of studies of the virus, its composition, and its relationship with disease. The studies continue and regularly produce new findings that may help in treating the results of infection and the causes of AIDS, or that may prevent the virus from infecting people.

Because all viruses rely for replication on the machinery of the cells they infect, their genetic material and structures are very simple. HIV is an RNA virus. Unlike all other living things, RNA viruses carry their genetic information on ribonucleic acid (RNA) and not deoxyribonucleic acid (DNA). HIV is a retrovirus, a type of RNA virus that, in order to replicate, must have its genetic information (carried on single-stranded RNA) converted to double-stranded DNA and integrated into the host’s DNA. This conversion is made possible by an essential and unique component of retroviruses, an enzyme called reverse transcriptase. When the genetic information from the virus is integrated, it is processed in the same way that the host’s genetic information is.

HIV infection begins when a structure on the viral envelope (the outer covering of the virus) attaches to a host cell by reacting with a CD4 antigen, which acts as a receptor on the host cell’s surface. CD4 receptors are particularly prevalent on the surface of CD4 T-lymphocytes. Recent evidence indicates that other receptor sites on cells also help the virus to attach itself. Another component of the viral envelope helps the virus enter the host cell. When the virus is within the cell, its reverse transcriptase converts the RNA of the viral core into DNA, and another enzyme integrates it into the host’s genetic information. The virus then may remain dormant for extended periods. Once it is activated, however, its genetic information instructs the host cell’s machinery to produce the essential proteins and the RNA, and directs the assembly of viral particles. The newly formed particles are then released from the host cell and are able to infect other cells.

Outside the body, the virus is reasonably sensitive to heat inactivation, depending on the medium in which it is present. Because the virus is covered by an envelope containing lipids (fatty acids), the virus can also be inactivated by treating it with a mixture of solvents and detergents.

The means by which the virus destroys the immune system are not yet completely understood. What is known is that the progression of the disease can be traced by measuring the decrease in the number of a patient’s CD4 T-lymphocytes. These lymphocytes are essential in the orchestration of an effective immune response. Among other functions, they help to regulate

antibody production by B-lymphocytes; they also stimulate the CD8 T-lymphocytes to kill infected or aberrant cells. CD4 T-lymphocytes perform these regulatory functions either by cell-to-cell interactions or through the release of chemicals called cytokines that regulate most aspects of the immune response.

Although there may be direct causal links between HIV infection and some cancers, such as non-Hodgkin's lymphoma, most of the manifestations of AIDS arise from the effects of the infection on the patient's immune system. When his or her immune response is suppressed, a person is more likely to succumb to the effects of infection by microorganisms that would otherwise be easily cleared from the body. Such infections are sometimes referred to as opportunistic infections.

In 1992, the United States Centers for Disease Control and Prevention in Atlanta, Georgia, published a "1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults." This classification scheme, shown in Figure 2.4, recognizes the various stages of HIV infection and the development of clinical symptoms. The symptoms of any one of the AIDS-indicator conditions listed in Figure 2.5, along with the presence of HIV or antibodies to HIV, are considered diagnostic of AIDS. In the revised classification, anyone who has HIV or antibodies to HIV and a CD4 T-cell (T-lymphocyte) count of less than 200 per microlitre of blood, regardless of the absence of AIDS-indicator conditions, is also considered to have AIDS.

The Centers for Disease Control's classification recognizes three stages of infection. After initial infection by HIV, there is a period (A in Figure 2.4) during which viral particles are actively produced and circulate around the body, especially in the blood. During this early phase, a person may experience mild general ill health, flu-like symptoms, and swelling of the lymph nodes called persistent generalized lymphadenopathy. The body's immune system responds to the presence of the virus: antibodies are formed and killer cells are activated. The length of time between initial infection and the development of detectable levels of antibodies varies from ten days to, perhaps, three months. This is the "window period" during which blood from a person who is infectious will not react in the initial tests for antibodies to HIV used to screen blood donations.

In the second phase (B in Figure 2.4), the infected person may or may not exhibit symptoms, and the infection appears to abate. Antibodies are detectable, varying levels of virus circulate, and there is a gradual decrease in the number of CD4 T-lymphocytes in the blood. Eventually most persons develop symptoms that are characteristic of AIDS, but the length of time before that happens varies. In the early 1980s, this latency period was thought to be in the range of two to four years. By the mid-1990s, it was thought to be as long as twelve years and possibly growing longer because of the effects of treatment.

Figure 2.4
1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults in the United States*

CD4 + T-cell categories	Clinical categories		
	(A) Asymptomatic, acute (primary) HIV or PGL**	(B) Symptomatic, not (A) or (C) conditions	(C) AIDS-indicator conditions***
(1) $\geq 500/\mu\text{L}$	A1	B1	C1
(2) 200–499/ μL	A2	B2	C2
(3) $<200/\mu\text{L}$ AIDS-indicator T-cell count	A3	B3	C3

* The shaded cells illustrate the expanded AIDS surveillance case definition. Persons with AIDS-indicator conditions (Category C) as well as those with CD4+ T-lymphocyte counts $<200/\mu\text{L}$ (Categories A3 or B3) became reportable as AIDS cases in the United States and Territories, effective 1 January 1993.

** PGL=persistent generalized lymphadenopathy. Clinical Category A includes acute (primary) HIV infection.

*** See Figure 2.5.

Source: Based on *Morbidity and Mortality Weekly Reports*, 18 December 1992

Figure 2.5
Conditions included in the 1993 U.S. AIDS surveillance case definition

- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical cancer, invasive*
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcer(s) (>1 month's duration); or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- *Mycobacterium avium* complex or *M. kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*, any site (pulmonary* or extrapulmonary)
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Pneumonia, recurrent*
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV

*Added in the 1993 expansion of the AIDS surveillance case definition

The third stage of the disease (C) is characterized by a generalized breakdown of immune defences and the onset of any of the indicator conditions listed in Figure 2.5. The length of time between the onset of AIDS and death is increasing as a result of new, combined therapies. Time will tell whether treatments will ever cure AIDS or at least render it not inevitably fatal.

The “case definition” used for surveillance of AIDS in Canada, like that used in European countries and Australia, and unlike that used in the United States, does not include the criterion of a CD4 T-lymphocyte count of less than 200 per microlitre of blood.

Our understanding of the role of the immune response in the development of AIDS is still evolving. Following HIV infection, there appears to be a constant and complex battle between the virus and the T-cells and antibodies that have been found, at least in the laboratory, to be capable of neutralizing the virus. It is thought that the highly variable nature of the virus affects this battle and explains the resistance that develops after some treatment. Recently, a strain of the virus has been discovered that is not reliably detected by the tests for antibody currently used in screening donated blood.

Hepatitis C and the hepatitis C virus

Hepatitis, or inflammation of the liver, is a disease that has been known for centuries. Many causes have been found for it, including toxic chemicals, therapeutic agents, and a number of microorganisms. The nature and course of the disease vary depending on the causative agent, the state of health of the person, and interactions of the many factors that affect the liver.

Patients were known to acquire hepatitis following blood transfusions soon after blood transfusions became widely used in the 1940s. During the 1970s, studies revealed that the hepatitis B virus could be transmitted in blood and was a significant cause of post-transfusion hepatitis. Screening tests were introduced to reduce the chance that blood from a donor with infectious hepatitis B would be used for transfusion. The screening proved effective for hepatitis B, but post-transfusion hepatitis still occurred. The recognition of non-A, non-B hepatitis resulting from transfusion is described in Chapter 22, as is the identification of the microorganism now known as the hepatitis C virus. What follows is a brief description of that virus as it is known in 1997.

The hepatitis C virus is an enveloped RNA virus, but it is not a retrovirus. During its replication there is no DNA intermediate, and the virus cannot be integrated into the host's genetic information. The virus has not been grown in a culture in the laboratory, but has been intensively studied using molecular biological techniques. It does not belong to the same family as other hepatitis viruses with the possible exception of the newly discovered hepatitis G virus, which may be closely related.

As in most viral infections, in the early stages of hepatitis C infection, a large number of viral particles are likely to be produced and the infection is acute. The immune system responds, and the virus may be cleared from the

body. It may not be cleared completely, however, and may remain dormant or may continue to infect new cells at a slower rate. This is chronic infection (long-term, and often at a low level) and may or may not be associated with chronic disease with long-term clinical manifestations.

Although the nature and organization of the genetic material of the hepatitis B virus (a DNA virus) and the hepatitis C virus are quite different, the two viruses share many clinical characteristics. Both are transmitted through blood. Acute infection may be associated with flu-like symptoms and jaundice, yellowing of the skin and eyes, especially in hepatitis B. Both viruses can cause chronic infection. Approximately 10 per cent of persons infected with hepatitis B remain chronically infected, and as many as 60 to 80 per cent of persons infected with hepatitis C have chronic infection. In the early stages of chronic infection persons show no symptoms, but often, after many years, they develop cirrhosis and sometimes liver cancer. As more is learned about the clinical manifestations of hepatitis C infection, it is becoming recognized as the most serious form of viral hepatitis; it accounts for the majority of liver transplantations in North America. Several clinical symptoms and conditions that do not appear to be directly related to liver damage are also being associated with chronic hepatitis C infection. Persons at high risk of being infected with hepatitis C include recipients of blood and blood products, intravenous drug users, and persons who have received tattoos or undergone body piercing. It is estimated that about 1 per cent of North Americans carry the hepatitis C virus, and that about 30 per cent of the carriers fall outside the high-risk categories. Although information about transmission from mother to fetus, by sexual contact, or by contact with other body fluids is still being analysed, the risk of transmission by these means appears to be low.

As with HIV and most other RNA viruses, mistakes can occur in the replication of the genetic material of the hepatitis C virus, leading to a high rate of genetic diversity. The resulting variations in strains may explain the resistance of the virus to drug therapy and its ability to avoid immune defences and to persist within the host. The potential number of strains or types also increases the difficulty of screening blood samples by using tests that rely on detection of specific antigens, usually those exhibited on the surface or envelope.

Because it is so often chronic, yet may cause only fairly mild symptoms in acute infections, the hepatitis C virus poses a significant threat to the safety of the blood supply. Specific tests for antibodies to hepatitis C, although significantly improved since they were first developed, are still only about 95 to 97 per cent sensitive – that is, three to five of every hundred infected blood samples will not show as positive. This low sensitivity is thought to result in part from the long time between the onset of infection and the development of detectable levels of antibodies. Variations in strains and other factors may also play a part.

PART II

The Canadian Blood System at the Emergence of AIDS

Introduction

The epidemics of AIDS and hepatitis C, both of which have brought tragic consequences for thousands of persons, assumed serious proportions during the 1980s. Among other methods of transmission, AIDS and hepatitis C were spread by the transfusion of blood components and the infusion of fractionated blood products. These infections have already led to hundreds of deaths in Canada and will lead to many more hundreds still.

To evaluate the efforts made to prevent or to minimize the spread of AIDS and hepatitis C through the blood supply during the 1980s, it is necessary to understand the historical and institutional context in which those efforts were made. The description of that context is focused, although not exclusively, on 1982, the year in which a relationship first was recognized between infection with AIDS and the use of blood components and blood products. The most important measures to prevent or to minimize the risk of AIDS and hepatitis C were taken after that year.

Each of the next six chapters describes a part of the historical context. The chapters describe in turn the operator of the blood supply system, the Canadian Red Cross Society; developments in the domestic fractionation industry, especially as they affected the supply of the fractionated blood products used in the treatment of hemophilia; the body through which the provinces funded the system, the Canadian Blood Committee; the regulator of the system, the Health Protection Branch of the federal Department of National Health and Welfare, and in particular its Bureau of Biologics; the public health systems, both provincial and federal, which had important roles to play in the prevention of disease transmission; and the evolution of the treatment of hemophilia, the risks associated with that treatment, and the national organization that represented hemophiliacs, the Canadian Hemophilia Society.

The expression "blood supply system" is used for convenience. The truth is that during the entire relevant period, no integrated system existed.

3

The Canadian Red Cross Society

Canada's national blood supply system has its roots in a wartime partnership between the Canadian Red Cross Society (Red Cross) and Connaught Laboratories (Connaught). The Red Cross is a not-for-profit humanitarian organization, established in 1896 as a branch of the British Red Cross Society and incorporated in 1909. During wars in which Canada was involved, the Red Cross served as an auxiliary to the medical services of the armed forces. In 1939, Connaught, which had been founded in 1914, was part of the School of Hygiene of the University of Toronto. Its operations were supported by the sale of products that it made and sold on a not-for-profit basis. It had considerable experience in producing biological products for medical treatment.

With the start of World War II, Connaught, to meet the need of the armed forces, successfully developed a method of producing dried human blood serum. Blood was collected into sterilized glass bottles and allowed to clot; the liquid serum that remained after clotting was separated and removed from the clotted material and was then processed and freeze-dried. In 1940, the Red Cross began to collect blood from volunteers to supply Connaught. Donations increased from 36,000 donations during 1941 to more than 890,000 during the last year of the war. At first, the Red Cross shipped the clotted whole blood, without processing it, directly to Connaught. However, as the volume of donations increased, the Red Cross did some processing – the removal of the liquid serum from the clotted material – at laboratories throughout Canada. In 1944, with Connaught's operation at full capacity, the Institut Armand-Frappier, then part of the Université de Montréal, also began to produce dried serum from donations collected by the Red Cross.

Developments at the Red Cross

The blood program developed by the Red Cross during the war was put to use when peace came. In 1945, the Red Cross decided to obtain whole blood from volunteers, collect it into bottles containing anticoagulant, store it, and provide it free of charge to hospitals. In 1947, it established a national blood transfusion service for that purpose. That year it opened its first blood centre, in Vancouver. By 1961, the Red Cross was operating sixteen blood centres,

serving every region of the country. A seventeenth blood centre opened in 1979. Most of the capital costs of establishing a centre were paid by the province in which it was located. The Red Cross paid the cost of equipment and the operating costs, including the salaries of the employees who operated the centres, from its own resources.

The blood processed by the blood transfusion service continued to come from volunteer donors, as it had during the war. Whether it was possible to recruit enough volunteer donors during peacetime to supply civilian needs throughout the country, however, was an uncertainty in 1945. By 1961, the efforts of volunteers in the Red Cross blood donor recruitment program and the generosity of Canada's volunteer donors had made this possibility a reality.

In the 1940s, 1950s, and 1960s, the Red Cross blood program was relatively simple. Red Cross volunteers recruited blood donors. Paid employees in the blood transfusion service then collected, tested for blood group and for syphilis contamination, stored the donated blood, and delivered it to hospitals. Although the work carried out by the employees of the blood transfusion service, which was nationally directed from its head office, was obviously essential, the dominant part of the Red Cross blood program during these decades was the work carried out locally by volunteers to recruit blood donors. During the early 1970s, the balance between the two parts of the program began to shift because of changes in transfusion medicine.

In the mid-1960s, two developments changed transfusion medicine substantially. They occurred more slowly in Canada than they did in the United States and much of Europe. The first was a technological advance – the production of sterile plastic bags that replaced the sterilized glass bottles in which blood had until then been collected and stored. Blood donations now were collected in a plastic bag that was linked by sterile tubes to other bags in a closed system. As a result, donations could be collected and processed within the system of bags, so that the blood could be separated into its constituent components – red cells, platelets, and plasma – without danger of contamination from exposure to air. Each component could be preserved at its optimal storage temperature, ranging from sub-zero for plasma to 22°C for platelets, thus extending the component's shelf life. As a result, fewer donors were needed to meet demand. Moreover, plasma could be separated from whole blood and frozen within hours of collection in order to preserve proteins of therapeutic value that would otherwise degrade quickly.

The second development was a gradual change in medical practice from the transfusion of whole blood to the transfusion of only the component required by the patient's clinical condition. This change became possible with the use of the plastic collection bag. Then, in 1964, it was realized that cryoprecipitate (that part of fresh frozen plasma that does not dissolve upon thawing), which was rich in factor VIII, the protein deficient in persons with type A hemophilia, was useful in the treatment of type A hemophilia. This

discovery transformed the treatment of this disease. Cryoprecipitate transfusions, because of their relatively high concentration of factor VIII, delivered factor VIII more quickly and in greater quantities than whole blood or plasma, and so reduced the risk of morbidity and mortality. Because factor VIII degrades quickly if plasma is not frozen soon after it is collected, the use of cryoprecipitate increased the demand for fresh frozen plasma, which in turn increased the demand for the separation of whole blood into components. Another development, the commercial production in the late 1960s of freeze-dried factor VIII concentrate, made from cryoprecipitate and containing factor VIII in an even more concentrated form than in cryoprecipitate, again transformed the treatment of type A hemophilia and again increased the demand for the separation of whole blood into components.

Although these developments occurred in the 1960s, it was only in 1970 that the Red Cross equipped two of its sixteen centres for large-scale production of components. The delay was caused in no small measure by a lack of funding. In order to carry out component separation, the Red Cross needed capital funding to obtain space for laboratories and to equip them with centrifuges for separation, freezers to freeze plasma and make cryoprecipitate, and other equipment to test the potency and sterility of components. It needed to obtain the space and equipment in which to store the components at their optimal storage temperatures. It also needed an increased operating budget in order to engage and train additional personnel.

For each of the blood-processing centres, this capital funding had to be obtained from the province in which the centre was located. Throughout the 1960s, 1970s, and 1980s, the Red Cross found it difficult to obtain sufficient capital funding from the provinces.

Funding for the increased operating budget of the blood transfusion service also proved difficult. From 1947 to 1958, the Red Cross paid operating costs itself, but, as the demand for its services increased and as its operations became more complex, that commitment eventually became an impossible burden. In 1958, it secured financial support from the federal and provincial governments under the *Hospital Insurance and Diagnostic Services Act*, which provided for the two levels of government to share equally in funding hospital expenses. The governments began collectively to pay 30 per cent of the operating costs of the blood transfusion service. Over the years their share increased, until it reached 90 per cent. Even that proved too little. By 1973, the Red Cross's 10 per cent of the blood transfusion service budget amounted to \$1 million, and expansion of component production was hampered because the Red Cross could not meet its share of the necessary increase in operating costs. In the words of Dr Roger Perrault, who became the national director of the blood transfusion service in 1974, “[t]his was a system that was hardly making it. The 10 per cent was bleeding the Red Cross dry.” In 1973, the governments agreed that beginning in 1974 they would pay 100 per cent of the operating costs. In 1977, with the enactment of the *Federal-Provincial Fiscal*

Arrangements Act, the federal government no longer paid 50 per cent of provincial hospital costs; that *Act* created complex formulas for the transfer of funds from the federal to the provincial governments for a number of programs, including postsecondary education, hospital costs under the *Hospital Insurance and Diagnostic Services Act*, and other medical care costs under the *Medical Care Act*. In 1984, the *Hospital Insurance and Diagnostic Services Act* was repealed and replaced by the *Canada Health Act*, which continued the complex formulas for the transfer of funds from the federal to the provincial governments for hospital costs. Although these statutes shifted the shares of the governments for the blood transfusion service's operating costs, collectively the federal and provincial governments continued to pay 100 per cent of those costs.

It is important to acknowledge the considerable resources that the Red Cross committed to the other part of its blood program, blood donor recruitment. Because almost all the work of blood donor recruitment was carried out by volunteers, the costs were kept to a minimum. For the costs that were incurred, the Red Cross paid 100 per cent until 1973. Thereafter, the governments contributed to that program also, 40 per cent of the costs beginning in 1974, rising to 60 per cent in 1975, and to 80 per cent in 1976.

Developments at Connaught

In 1947, the Red Cross began to supply hospitals with whole blood. Blood that was not used by the hospitals before its expiry date was given to Connaught for processing. Connaught separated the liquid plasma from the cellular components and used it to produce dried plasma, which replaced dried serum as a therapeutic agent. In October 1954, Connaught opened a modern plasma fractionation plant that allowed it to make new blood products. The cost of the plant, \$400,000, was paid by both the Department of National Health and Welfare and provincial health departments. The Red Cross continued to supply Connaught with whole blood that had passed its expiry date. Connaught continued to separate the plasma, but now, instead of drying the plasma, Connaught fractionated it into some of the hundreds of proteins it contained. The fractions derived from the process were refined to produce therapeutic blood products. At first, Connaught produced three fractionated blood products: immune globulins, containing antibodies to fight disease; fibrinogen, used to enhance clotting; and albumin, used in place of dried plasma to fight shock. These products were distributed to hospitals free of charge by the Red Cross. (Blood components and products and their therapeutic uses are described more fully in Chapter 2.)

For more than half a century, Connaught was able to finance its operations from the revenue generated by the sale of the biological products it made, even though it sold them at prices below market rates. By the early 1970s, however, it was no longer able to do so. Prices for vaccines, from which Connaught obtained most of its revenue, had fallen, and with them the resources necessary

for reinvestment. Connaught's physical facilities deteriorated and the value of its intellectual capital – its methods of production and its marketable products – depreciated. Although the laboratory's scientific research continued, there was a dearth of investment in applied science for the development of new or improved products. The fractionation plant became too small to meet the demand for blood products, and its equipment became outdated. At a time when commercial fractionators were surging ahead in the development of new blood products, Connaught lagged. The University of Toronto recognized the need for investment, but did not feel that educational funds should be used for the purpose. The Ontario government refused a request for financial assistance. In June 1972, the university sold Connaught to the Canada Development Corporation, which had been established by the federal government in 1971 with three purposes: to develop and maintain strong Canadian-owned and managed corporations in the private sector, to widen investment opportunities for Canadians, and to make a profit for its shareholders. Connaught then became a for-profit corporation.

By 1972, Canadian hemophiliacs and their physicians were beginning to demand that the Red Cross supply factor VIII and IX concentrates for the treatment, respectively, of type A and type B hemophilia. On 14 June 1972, Hyland Therapeutics Division of Travenol Laboratories Inc. (Hyland), a U.S. commercial fractionator, offered to supply the Red Cross with these products. The Red Cross told Connaught of the offer on 19 June, with the comment: "Although we do not like to admit it publicly, especially to the [Canadian] Hemophilia Society, I believe the time has now come for the Canadian Red Cross Blood Transfusion Service to produce, or at least have on hand, a quantity of AHF [anti-hemophilic factor] concentrate." Connaught replied on 14 July that there was "a good possibility" that it could supply factor VIII concentrate, but did not say when it might be able to do so. In fact, it took Connaught several years to develop and produce licensed factor concentrates. The obstacles it met are described in Chapter 4, as are the proposals made and the steps taken by the Red Cross to obtain fractionated blood products from manufacturers other than Connaught.

Improvement of the blood transfusion service

When Dr Perrault became the national director of the blood transfusion service in 1974, he said that it was "15 to 20 years out of date" and "behind many European and American centres in terms of technical and professional development and standing." He set out to achieve two basic goals for its improvement. The first was to find physicians who would serve as full-time medical directors of the local blood centres, since the blood transfusion service needed medical leadership to encourage research and carry out innovations within the system. Until 1974, there had been only one full-time medical director at any Red Cross blood centre. That was Dr Perrault himself, from 1972, at

the Ottawa centre. His second goal was to acquire the resources needed to continue to expand component production. Until all donated blood was being processed into components, the service would be distributing a less than modern product – whole blood – to hospitals.

By 1982, Dr Perrault had assembled a cadre of medical directors to run the blood centres. It has been difficult to attract good candidates to work exclusively in the blood centres, because the best candidates wanted to continue their work in local medical schools and hospitals. In order to overcome this difficulty, the Red Cross created the position of "major part-time" medical director in 1974. The primary responsibility of such officers was that of medical director, but they were only expected to serve at least 50 per cent of their working time in the centres. By 1982, the directors who spent half or more of their working time in the centres were no longer distinguished from those who spent all of their working time there, and all came to be regarded as "full-time" directors. In that year, "full-time" medical directors were in charge of fifteen of the seventeen blood centres.

Because they were allowed to spend as much as half their time outside the centres, the medical directors could seek cross-appointments in local medical schools. They were encouraged to do so by Dr Perrault in order to open research opportunities and to build contacts through which to educate physicians about transfusion medicine. Most of them successfully sought cross-appointments. The opportunities for research gained in this manner were important because the blood transfusion service had no research budget of its own until 1983.

In order to carry out the expansion of component production, Dr Perrault had to obtain very large budgetary increases. The blood transfusion service's budget for the local centres rose from approximately \$9 million in 1973 to \$21 million in 1976, \$35 million in 1979, and \$52 million in 1982. By 1982, 90 per cent of the donations collected were being transformed into components. By 1984, almost all were. The increases in the budget were reviewed and approved by the Federal-Provincial Program and Budget Review Committee (originally, the federal-provincial budget and program review sub-committee of the advisory committee on institutional and medical services). That committee, which reported to the federal and provincial deputy ministers of health, was formed in 1973, when the governments decided to pay 100 per cent of the blood transfusion service's operating costs. The committee reviewed the blood transfusion service's annual budget and allocated shares of it to each province. This budget covered the cost of component separation, but it did not cover the cost of fractionation to make blood products. Blood products were paid for by each province according to the amount it used. The committee also fixed the prices to be paid by the provinces for the fractionated blood products distributed by the service. At first, the committee was composed of civil servants representing western Canada, Ontario, Quebec,

and Atlantic Canada; in November 1979, Quebec withdrew, and the Red Cross was thereafter required to submit a separate budget to that province for the work done by its blood transfusion service there.

Dr Perrault had, by and large, achieved both his basic goals by 1982. Before long the blood transfusion service would provide only modern components to hospitals, and all except the two smallest blood centres were led by full-time medical directors. Canada no longer had a blood transfusion service that ranked behind those of other nations.

There remained one major gap in the service's production of components. In April 1978, the service had begun to make fresh frozen plasma that could then be fractionated to produce blood products. The amount of fresh frozen plasma it produced was, however, insufficient to meet the domestic demand for factor VIII concentrate. As a result, the Red Cross had to buy factor VIII concentrates that were made from U.S. plasma, most of which was collected from persons paid for their plasma rather than from volunteer donors. One reason for the shortage of fresh frozen plasma was that much of the whole blood donated in Canada was collected in mobile clinics that were some distance from one of the blood centres; fresh frozen plasma could be made only from whole-blood donations collected close to the centres, for only then could plasma be separated from the whole blood and be frozen before the biological activity of the factor VIII deteriorated significantly. By 1982, 84 per cent of whole-blood donations was collected in clinics close to a blood centre, an increase from 55 per cent in 1974, and that proportion grew to 93 per cent by 1984. There was thus little more that the blood transfusion service could do to increase its supply of fresh frozen plasma by changing the location of its clinics.

Some years earlier the blood transfusion service had begun to deal with the other major impediment to its supply of fresh frozen plasma – its dependence on donations of whole blood. To do so it looked to an alternative process called plasmapheresis, by which donors could give only plasma and do so in greater quantities and more frequently than was possible through the collection of whole blood. (The process is described more fully in Chapter 2.) The blood transfusion service conducted a plasmapheresis trial at the Ottawa and Montreal blood centres in 1978. It determined that donors who gave plasma through plasmapheresis experienced no adverse effects and that the plasma collected was high in factor VIII. In 1979, it began a small-scale plasmapheresis program, using the plasma to make fresh frozen plasma. In 1980 and 1981, the Red Cross proposed budget increases that would allow it to expand its plasmapheresis operations. The funding approved by the Federal-Provincial Program and Budget Review Committee fell well below what was necessary, however. In 1982, after the approval of funding that met 76 per cent of the budget for plasmapheresis collection proposed by the Red Cross, the blood transfusion service was able for the first time to increase significantly its collection of plasma by this process. Nevertheless, the total

amount of fresh frozen plasma produced from both whole-blood and plasmapheresis donations in 1982 was only approximately 50 per cent of the amount required for self-sufficiency. This was not an unusual situation; few countries have been able to meet their domestic demand for fresh frozen plasma through voluntary donations, and most have had to depend on the purchase of concentrates made from plasma obtained from persons who were paid. After 1982, the Red Cross continued to seek domestic self-sufficiency in fresh frozen plasma through expanded plasmapheresis operations, but continued to be frustrated by inadequate funding.

The organizational structure of the Canadian Red Cross Society in 1982

In 1982, the blood transfusion service was one of several programs embedded in the organizational structure of the Canadian Red Cross Society. The Canadian Red Cross Society was a member of an international organization, the League of Red Cross Societies (league), which later became the League of Red Cross and Red Crescent Societies. The members of the league were the national Red Cross societies throughout the world.

The league is distinct from the International Committee of the Red Cross (international committee). The international committee was established under Swiss civil law. Under the four Geneva Conventions of 1949 and their additional protocols of 1977, it has certain powers during times of armed conflict. These powers allow the international committee to encourage compliance with the humanitarian standards found in the Geneva Conventions and to provide humanitarian relief to the victims of war, both military and civilian.

In 1965 the league proclaimed seven fundamental principles, which were subsequently incorporated into the letters patent of the Canadian Red Cross Society. The language defining the principles has been amended from time to time, but with no substantial change in meaning. In 1982, they read as follows:

Humanity: The Red Cross, born of a desire to bring assistance without discrimination to the wounded on the battlefield, endeavours – in its international and national capacity – to prevent and alleviate human suffering wherever it may be found. Its purpose is to protect life and health and to ensure respect for the human being. It promotes mutual understanding, friendship, co-operation and lasting peace amongst all peoples.

Impartiality: It makes no discrimination as to nationality, race, religious beliefs, class or political opinions. It endeavours to relieve the suffering of individuals, being guided solely by their needs, and to give priority to the most urgent cases of distress.

Neutrality: In order to continue to enjoy the confidence of all, the Red Cross may not take sides in hostilities or engage at any time in controversies of a political, racial, religious or ideological nature.

Independence: The Red Cross is independent. The National Societies, while auxiliaries in the humanitarian services of their governments and subject to the laws of their respective countries, must always maintain their autonomy so that they may be able at all times to act in accordance with Red Cross principles.

Voluntary Service: The Red Cross is a voluntary relief organization not prompted in any manner by desire for gain.

Unity: There can be only one Red Cross Society in any one country. It must be open to all. It must carry on its humanitarian work throughout its territory.

Universality: The Red Cross is a worldwide institution in which all Societies have equal status and share equal responsibilities and duties in helping each other.

Three aspects of these principles deserve special attention. First, the principles of impartiality and neutrality, as defined by the league, refer to action that would tend to discriminate against individuals on the basis of their race or nationality or to cause controversy about a group of people. This became important for the Canadian Red Cross Society and its blood program when two groups, Haitians and gay men, were identified as being at high risk of contracting AIDS and it was proposed that they be excluded from donating blood. The question then arose whether they could be excluded – and, if so, how it should be done. Second, the principle of independence, as defined, raised a question about the degree of government supervision of the blood program that the society would tolerate. These issues are considered elsewhere in the Report. The third principle, of voluntary service, created tensions between the employees of the blood transfusion service and the rest of the society. These tensions increased as the blood transfusion service grew.

In the 1980s, the Canadian Red Cross Society was controlled by volunteer members. From its inception, it had been dedicated to voluntary service. Although paid employees were hired to carry out certain tasks, they were employees of the volunteers who controlled the organization. The society was organized on a regional basis; local branches were controlled by ten provincial divisions, which in turn were controlled by the national organization, as was required by the principle of unity.

The names of the key bodies and officers of the Canadian Red Cross Society changed from time to time. In 1982, the society held an annual meeting (previously called the central council) of national members, three from each of the ten divisions who had been elected at the divisional annual meetings to represent the interests of their division at the national meeting. At that national meeting, officers of the organization were elected. They were the president (formerly the chairman), the vice-president (formerly the president), the

treasurer, the counsel, the chair of the national planning and budget review committee, the chair of the national blood transfusion service advisory committee, the vice-chair of the national blood transfusion service advisory committee, and the chair of the national field services committee. The officers, the immediate past president, and eleven to fifteen other persons who were elected (one representative from each of the ten provincial divisions, and one to five other persons) formed the board of directors (formerly the national executive committee). There was also an executive committee of the board of directors (formerly the sub-executive committee of the national executive committee), which included eight members of the board of directors (the president, the vice-president, the treasurer, the counsel, the chair of the national planning and budget review committee, the chair of the national blood transfusion service advisory committee, the chair of the national field services committee, and the chair of the national representative members). All of these positions were filled by senior volunteer members of the society. In order to assist the board of directors in day-to-day operations, the society employed a secretary general (formerly the national commissioner), who was directly responsible to the board.

It was not only at the national level that volunteers were important. At the grassroots level, they were the heart of the society's programs, of which the blood program was only one. The society participated in international programs, including development and disaster relief projects, and in assisting the International Committee of the Red Cross in its work. It operated several domestic programs, including emergency services (providing assistance after disasters), water safety services (providing training to reduce drowning and water-related injuries), first aid services (providing training in the treatment of injuries), and homemaker services (providing an alternative to institutional care).

Within the blood program, volunteers were at the centre of the blood donor recruitment program. The most important functional unit in that program was the local branch, since local volunteer workers recruited local volunteer donors. The national society was also involved in blood donor recruitment, assisting and coordinating the local volunteer effort. There was a national coordinator of blood donor recruitment and a national blood donor recruitment committee (disbanded in 1986, when it became a subcommittee of the national blood transfusion service advisory committee). In 1982, the committee was made up of both volunteers (the chair, the vice-chair, one representative from each of the ten divisions, the society's president, its honorary adviser in medical affairs, the chair of the national blood transfusion advisory committee, and one or two members at large) and employees (the secretary general, the national director of programs, and the national coordinator of blood donor recruitment).

The work of the other part of the blood program, the blood transfusion service, was carried out almost exclusively by employees, although a key volunteer committee was related to it. From the inception of the blood transfusion service, a committee of volunteer experts (medical and scientific professionals) provided advice to the board of directors. This national blood transfusion service advisory committee (called the national blood services committee after 1987) reported to the board of directors about the operations of the blood transfusion service and gave advice to the service's national director. Its chair and vice-chair were elected officers and members of the society's board of directors; the chair was also a member of its executive committee. The opinion of the chair was highly valued by the non-medical members of the board of directors. On any particular issue, therefore, it was important for the national director of the service to convince the committee of his opinion if he wanted a proposal to be accepted by the board of directors.

By 1982, the blood transfusion service consisted of its national office and the seventeen local blood centres. Every province had at least one blood centre, although only limited services were directly available in Charlottetown; most of the services for Prince Edward Island were provided by the Halifax blood centre. Services for the territories were provided by the blood centres with the most convenient air transportation links.

Every blood centre, other than that in Charlottetown, provided "core" services (the collection of donations; the processing, testing, and storage of the donations; and the distribution of blood components and fractionated blood products to hospitals). Blood components and products were distributed to hospitals on demand, unless, of course, there was no available stock. The medical directors did not decide whether a patient received a particular component or product. However, when requested, as they often were, the medical directors were available to give advice on the proper use of components and products, and in 1980 the blood transfusion service published the first edition of its *Clinical Guide to Transfusion*. The blood components distributed by a centre were usually made from blood collected by that centre. More generally, the components distributed were almost always made from blood collected within the same province. The regular exceptions were the services provided to the territories, services provided to Prince Edward Island from Halifax, services provided to northwestern Ontario from Winnipeg, and services provided to northeastern British Columbia from Edmonton. Otherwise, blood was usually transferred from one province to another only if there was an emergency. More regular transfers between provinces could have been used to ease local shortages, but they were resisted because every province paid for the operation of the blood transfusion service within its own borders and transfers of blood required concomitant adjustments of budget allocations. As a result, the inventory of collected blood was managed as nine separate entities rather than as one national resource.

Some blood centres also provided "non-core" services. For example, the Winnipeg blood centre provided cross-matching services (ensuring that a particular component was compatible with the blood of the prospective recipient) for hospitals in and near Winnipeg. Because such services were "non-core," they were paid for directly by the individual province rather than from the national blood transfusion service budget.

Each of the blood centres except the one in Charlottetown had a medical director (responsible for all operations at the centre), an administrator (responsible for non-medical administration), a nursing supervisor (responsible for clinics where donations were collected), and a technical supervisor (responsible for the testing, processing, and storage of the donations in the centre's laboratory). The blood centres did not have their own public relations staff, but had access to the public relations staff at the national and divisional levels. The public relations staff was to be important to the blood transfusion service after the emergence of AIDS. The general function of the public relations department was to keep the name of the Red Cross in good repute and high profile to assist its fundraising efforts.

Within the blood transfusion service, the medical directors of the local blood centres reported to the assistant national director at the national office of the blood transfusion service. The assistant national director reported to the national director, who reported to the secretary general of the society (its highest paid employee), who reported to the board of directors (the highest-ranking volunteers of the society). Medical directors had only limited opportunity for local innovation. National policies were being developed in an attempt to ensure uniform standards throughout the country, and the medical directors were expected to adhere strictly to those policies that were in place. Innovation was allowed only if a gap in national policy existed.

To assist in the administration of the blood transfusion service, annual meetings were held, beginning in 1981, of the medical directors and personnel from the national office. These were business meetings about the operation of the service, and a large number of topics were covered in the time allotted, usually two days; the meetings were not intended for discussion of scientific developments or research in detail, although there was limited discussion of scientific developments in the business context. More frequent contact between some medical directors and the national staff occurred through "working groups"; there were both standing working groups to consider issues and ad hoc working groups to consider emerging issues.

The balance between the two parts of the blood program began to shift during the early 1970s. Although donor recruitment remained vitally necessary, the growing sophistication of the blood transfusion service made it increasingly the more dominant part of the program. This change created problems that lasted into the 1980s. At the national level, the volunteers felt that the blood transfusion service staff, in its efforts to raise the service to

world standards, had not shown sufficient respect for the ultimate control of the volunteers. The potential for conflict was described in a memorandum by the assistant national commissioner to the national commissioner on 8 August 1979:

You asked me to prepare a list of the areas in which I felt there were difficulties existing between the National Office and the BTS [blood transfusion service]. I presume that you intended to include relationships between the BTS and the Divisions and Branches as well ...

Essentially, all of the questions which are included in this summary boil down to a major philosophical question – the question of the position of the BTS within the National Society. The BTS conceives of itself as a virtually independent unit, operating only within the name and symbol of the Red Cross, and with only a cursory bow to the Central Council once a year ...

Arising from this attitude come differences in interpretation as to authority and responsibility, lapses of communication and conflicts over "interference." All of these appear to be caused by the two contrary conceptions of the BTS; on the BTS side it being conceived of as a virtually autonomous body, and from the point of view of the rest of the Society as one of the Society's most crucial parts.

At the moment, the National Office and the Divisions and Branches consider the BTS to be part of the Society, and subject to all of the controls applied to other programmes of the Society. This is the historic situation, and until the Society deliberately chooses to change this situation I believe that we at National Office must continue to attempt to carry out our responsibilities based on this assumption. However, the tremendous growth in the Blood programme over the past six years has given rise to the present "autonomy" question with the BTS feeling that they are free to handle their affairs their own way, while the rest of the Society believes that they should be part of our mainstream programming.

Out of this situation arise difficulties at the National level in the area of budget, labour relations, and compensation, and at the Division and Branch level of physical facilities, allocation of overhead to BTS, orientation of BTS staff to the Society's general programmes, etc. In my opinion, very little progress will be made on any of the detailed problems until the more basic question of the orientation and position of the BTS within the Society is settled.

The relationship between the national office of the blood transfusion service and the volunteer divisions and branches was not an easy one. In particular, it was difficult for the nationally directed blood transfusion service to interact with the ten divisions and dozens of branches of the local volunteer effort

to recruit blood donors. The "tremendous growth" referred to in the memorandum was indeed impressive. The total budget for the seventeen blood centres and the national office of the blood transfusion service, including its national laboratory, grew from approximately \$12 million in 1974 to approximately \$74 million in 1982, and by that time accounted for 57 per cent of the Red Cross's total expenditures for international and domestic programs. The entire blood program budget, including blood donor recruitment, was approximately \$81 million, 62 per cent of the Red Cross's total program budget.

Problems also arose because the efforts of the blood centres, which were directed by the national office, were not always well coordinated with the local efforts to recruit blood donors. This was particularly true in Toronto, where the blood centre had to coordinate its efforts with the twenty-eight individual branches in its collection area that were recruiting donors. The structure that resulted was so complicated, and the difficulties of coordination so great, that the Toronto blood centre was unable to meet a steadily increasing demand for blood components during the 1980s. The situation was described in a 1985 internal Red Cross memorandum:

Most important, poor utilization of financial and human resources exists in a number of areas caused by an unnecessarily complex organizational structure and lack of a single accountability and leadership for the performance of the blood programme:

- The level of current funding and the current method of budget presentation give the impression that there are sufficient funds to carry out all Blood Programme functions with paid staff.
- The dichotomy of the system does not permit optimum utilization of Blood Centre resources. Decisions on the use of financial and human resources of the Blood Centre (\$10 million annually) are driven by a poorly controlled \$2 million dollar BDR [blood donor recruitment] operation.
- The lack of a single accountability combined with almost total absence of management information systems has led to ineffective political solutions and resulted in a profusion of committees.

Problem solving has been restricted to attempts by individuals and individual groups to resolve single issues without considering the total context of the Blood Programme.

Many individuals and individual groups working within the Central Ontario Blood Programme can be highly commended for their efforts. Although individual elements of the Programme are well controlled, the Central Ontario Blood Programme as a whole is currently unmanaged and lacks common control. [Emphasis in original.]

It was not until the late 1980s that solutions to this problem began to be implemented, through the gradual integration of blood donor recruitment into the blood transfusion service administrative structure.

Organizations in the United States

Although the operation of the blood supply system in the United States was different, actions taken there had a significant impact on events in Canada. In describing the events of the 1980s, there will therefore be frequent reference to certain U.S. organizations. These are described in greater detail in Chapter 27, which reports the response in the United States to threats to the blood system.

The U.S. system was pluralistic. The American Red Cross collected approximately half of the whole blood donated in that country. It was a not-for-profit, congressionally chartered organization, financially self-supporting through monetary donations and cost recovery. Cost recovery was possible in the United States because hospitals there, unlike those in Canada, paid for the blood components and products delivered to them and then charged the cost to their patients. Like its Canadian counterpart, the American Red Cross operated many programs unrelated to blood.

The remainder of the whole blood donated in the United States was collected by community blood centres and hospital blood banks. Community blood centres were freestanding organizations, nearly all not for profit, governed by volunteer boards, with the single function of providing blood components to hospitals in their communities. Local interests and history, rather than any plan, influenced their development and success. Some blood centres were able to provide all the blood components needed by hospitals in their communities; some were able to fulfil that need and to supply components to hospitals outside their communities; others were unable to meet local demand, and the hospitals in their communities had to look to other sources. Hospital blood banks usually collected blood donations only for their own hospitals. Very few collected enough to meet their total needs.

Two umbrella organizations for blood banks existed in the United States. The American Association of Blood Banks, established in 1947, was a not-for-profit organization interested in blood and tissue banking and in transfusion and transplantation medicine. In 1982, it had more than 2,000 accredited institutional members (blood centres, hospital blood banks, and hospital transfusion services) and more than 6,000 individual members. It operated a voluntary accreditation and inspection system that helped blood banks and transfusion services to evaluate their own operations against established standards. Its members collected almost all the whole blood donated in the United States. In 1962, the Council of Community Blood Centers, established in 1962, represented the common interests of twenty-seven independent, not-for-profit community blood banks that were unaffiliated with the American

Red Cross. It was governed by a board of directors consisting of one representative from each institutional member. One of its services was the publication of a weekly newsletter.

Most of the plasma collected in the United States was obtained, using plasmapheresis, from persons who were paid for their plasma. Many persons had their plasma collected weekly. The plasma was collected by four large U.S. fractionators or their affiliates and other commercial operators. The other commercial operators sold most of what they collected to the U.S. fractionators. The fractionators used the plasma they collected themselves and that they purchased from others to make blood products, such as the factor concentrates used in the treatment of hemophilia. The American Blood Resources Association, a trade association founded in 1971, represented 80 per cent of the commercial plasma collectors and all four of the U.S. fractionators.

4

The Search for Self-Sufficiency in Fractionation

In 1972, Connaught Laboratories Limited (Connaught) was the custom fractionator for the Canadian Red Cross Society (Red Cross). The Red Cross sent the plasma it derived from blood donations to Connaught to be processed (fractionated) into various blood products, which were then returned to the Red Cross for distribution throughout the country for use in medical treatment. This relationship, based on an unwritten agreement, was open and cooperative – as it had been since the 1940s. The system had not kept pace with medical developments, however, and through the courses of action pursued to satisfy national requirements, the former partners became increasingly bitter rivals. During the mid-1970s, both organizations proposed building large modern fractionation plants to supply therapeutic blood products. In the end, neither proposal was implemented, and Canada was left without a fractionation plant that could meet its needs.

The inadequacies of the blood system in this period were identified by the Canadian Hematology Society, a body founded in 1970. Its members were physicians and scientists who were concerned with the diagnosis, care, and treatment of children and adults with blood-related diseases and with the management of hematology laboratory services. In May 1971, the society had created an ad hoc committee to study the needs for whole blood, blood components, and blood products in Canada, to examine whether the Red Cross was capable of meeting those needs, and to recommend steps to fill the gaps between needs and capability. The committee reported in November 1972. Its review of the Red Cross was positive with regard to the blood donor recruitment program, but was more critical of the blood transfusion service. The committee found that the Red Cross was not providing the full range of therapeutic blood products, including the factor concentrates used in the treatment of hemophilia, and was not providing adequate supplies of blood components. It recommended that the Red Cross improve its centres and “inculcate the ‘production’ concept” internally so that it could supply the full range of blood components and products needed for modern medical needs. It also recommended that a new or second fractionation plant be built if

Connaught's was incapable of producing the full range of products. In particular, the committee was concerned about the need for factor VIII and factor IX concentrates for the treatment of hemophilia.

The Canadian Hematology Society accepted the committee's report, and in January 1973 made certain findings and recommendations to the Red Cross. Although it found the blood transfusion service to be "a sound structure and a valuable national resource," it recommended that it adopt as an objective the provision of the full range of therapeutic blood products through production or purchase, and that it hire full-time professional staff dedicated to meeting this objective as quickly as possible.

Fractionation at Connaught

By the time the Canadian Hematology Society had issued its report, Connaught was already starting to produce new fractionated blood products. It began with factor IX concentrate, used in treating hemophilia B. Demand for factor IX concentrate was not as great as that for factor VIII concentrate, used in treating hemophilia A, but its production was less complex. Equally important at the time, the raw material was more readily available. Because the factor IX protein is relatively stable, the concentrate could be made from "stored plasma" that had not been frozen immediately after collection. Production of factor VIII concentrate, in contrast, required fresh frozen plasma, which was then in limited supply. By December 1972, Connaught was producing small quantities of factor IX concentrate from stored plasma supplied by the Red Cross and was authorized to distribute it for clinical trials. Those trials took time, but in June 1975 Connaught applied for a licence for general distribution.

Blood products made from stored plasma always carry a risk of pyrogenicity – the presence of fever-causing substances. The risk is lower with plasma that has been fresh frozen, but in the mid-1970s the Red Cross needed all the fresh frozen plasma it could produce to make cryoprecipitate, which was used in the treatment of hemophilia A. Inevitably, some of Connaught's factor IX concentrate proved to be pyrogenic. Entire production lots had to be destroyed, thereby lowering average yields and increasing unit costs.

Connaught's ability to make factor VIII concentrate progressed slowly. It did not find a person with the necessary expertise to lead its development project until November 1973. In August 1974, it asked the Red Cross for a supply of fresh frozen plasma so it could move towards clinical trials, but again the Red Cross had none to spare. Connaught then turned to the Winnipeg Rh Institute Inc. (Rh Institute), a not-for-profit corporation engaged in the development and small-scale production of blood products, which was already supplying Connaught with fresh frozen plasma to make some specialized blood products. One of these products was tetanus immune globulin, for which the Rh Institute collected plasma from persons who had been immunized against tetanus. The institute agreed that Connaught could use

the hitherto unused cryoprecipitate from this fresh frozen plasma to develop its factor VIII concentrate process. It proved significant, later, that this plasma came from persons who were paid for their plasma. On 1 October 1975, Connaught applied for authorization to conduct clinical trials of its factor VIII concentrate.

While investing in the development of its factor VIII concentrate, Connaught had assumed that its relationship with the Red Cross would continue and that it would remain the sole custom fractionator for the Red Cross, and thus the sole fractionator for the nation. It did not question this assumption even when the Red Cross refused to supply fresh frozen plasma, because the reason given was short supply rather than any breakdown in the relationship. Nevertheless, the Red Cross was the only significant domestic source of plasma, and without an assured supply of fresh frozen plasma from that source, Connaught hesitated to carry out the necessary renovations to its fractionation plant (Building 50). Connaught's hesitation was consistent with a view expressed by Dr Roger Perrault, the national director of the Red Cross blood transfusion service, in analysing another fractionation proposal: "[I]n plasma fractionation technology, the most important aspect is the procurement of plasma, and not the construction of a plant." Connaught did make some renovations to Building 50 in 1975, but not enough to bring it to then current standards. Hard-to-clean surfaces and the open design of the processing equipment were incompatible with sterility in the blood processing system; modern monitoring equipment was absent; and the equipment was small in scale.

On 5 November 1975, the Red Cross told Connaught that it would deliver an estimated 50,000 litres of fresh frozen plasma in 1977 and 150,000 litres in 1978. Those figures might have been enough to induce Connaught to improve its plant further. However, by then it was becoming apparent that the Red Cross had fractionation aspirations of its own, and that the deliveries might not be made. Connaught began to press the Red Cross for a written long-term contract, ensuring adequate supplies of fresh frozen plasma.

Red Cross plans for fractionation

Soon after taking office as the national director of the Red Cross blood transfusion service in 1974, Dr Roger Perrault sought to expand the Red Cross's role in the Canadian blood system. He wanted it to be able to do everything necessary to meet the domestic demand for blood components and therapeutic blood products. The Red Cross would collect donations and convert them into the full range of components at its own modern blood centres, manufacture the full range of therapeutic blood products in its own modern fractionation plant, and provide, free of charge to hospitals, all the blood components and therapeutic blood products needed to meet Canadian demand. In the autumn of 1975, he proposed that the Red Cross build a fractionation plant.

Dr Perrault's approach fitted closely with international views of the time. In the early 1970s, the League of Red Cross Societies, of which the Canadian

Red Cross Society is a member, had alerted the World Health Organization to a transfusion-related health concern. Commercial fractionators were buying plasma from persons in developing countries irrespective of the state of their health; this practice posed a risk both to those paid for their plasma and to the recipients of blood products made from it. Preliminary inquiries by the World Health Organization indicated that there was indeed "an extensive trade in human blood and its derivatives in many countries," and in May 1975 the organization passed a resolution that, among other things, urged its member states "to promote the development of national blood services based on voluntary non-remunerated donation." The hope was that, as more countries became self-sufficient by collecting enough plasma from volunteers to meet their domestic demand for blood products, the incentive for commercial firms to pay persons in developing countries for their plasma would decrease. Two months later, the same concerns were expressed by the International Society of Blood Transfusion, which consists of professionals from blood banks, medical schools, laboratories, hospitals, and pharmaceutical companies. It urged all governments to develop domestic blood transfusion services that collected enough donations from unpaid donors to meet domestic needs.

In the autumn of 1975, Dr Perrault retained Dr John Watt to report on how the Canadian Red Cross Society could best supply the full range of therapeutic blood products. Dr Watt was the scientific director of a fractionation plant that was an integrated part of the Scottish National Blood Transfusion Service. He delivered a preliminary report on 29 October 1975. In his opinion, from his observations in several countries,

the most effective blood transfusion services carry out the complete function of procuring blood and its components, both molecular and cellular. Those countries which fail to bring the complete clinical service into one collaborative effort, with logistical integration under the managerial control of a single office and with procurement and delivery of blood and its components through the same clinical service, fail also to provide an adequate service to hospital and other physicians. Observation of the situation now pertaining in Canada has not altered this opinion but has, rather, served to strengthen it since much of the failure to deliver an adequate service in Canada stems directly from the fragmentary nature of the system now in operation.

In his analysis of the Connaught–Red Cross relationship, he said:

Strong, and I believe overwhelming, arguments can be advanced on why this arrangement should be phased out and discontinued ... Chief among these is the effect of breaking the motivation to achieve direct supply of clinical need which can be created if a flexible policy of supply and demand

is coordinated through a single agency. Commercial interests have the effect of producing inflexibility in process design and purpose and this inflexibility is inimical to effective clinical supply. A good example of this already exists in Canada where, despite a reasonably good personal relationship and realistic attempts to achieve a community of purpose, new plasma fractions have been requested from Connaught over more than a decade and remain unavailable from within Canada. The result of this is that no concentrate exists for the treatment of hemophilia A or B.

He recommended that the Red Cross create a fractionation plant of its own that would be adequate to supply the total domestic need for therapeutic blood products.

On 3 December 1975, the Red Cross blood transfusion service held an extraordinary meeting of the volunteer experts on its scientific advisory committee to discuss domestic fractionation. The topic is described in the minutes of the meeting as urgent. The nature of the urgency is not identified in the minutes but is clear from other documents. The Red Cross was in the midst of contract negotiations with Connaught, which wanted a five-year agreement for the supply of plasma and the distribution of concentrate as a precondition to modernizing its plant. If the Red Cross was going to build its own fractionation plant, it did not want to enter into any such long-term agreement, for it was unlikely that governments would support construction of a Red Cross plant if a modernized one already existed at Connaught. The scientific advisory committee agreed with Dr Watt's view that the "present arrangement is inadequate" and endorsed his recommendation that the Red Cross "establish a national fractionation centre."

Later that month, the World Health Organization and the League of Red Cross Societies held a five-day meeting in Switzerland to discuss the implementation of the May 1975 resolution regarding "voluntary non-remunerated donation." One of the recommendations from that meeting, made unanimously, was that whole-blood donation and supplementary plasmapheresis (to the extent that it was necessary for national self-sufficiency in plasma) should be voluntary and unpaid. Further, a "general agreement" was reached that

[t]ransfusion services should be completely independent of any control by commercial interests. Although in certain parts of the world it may still be necessary to enlist the cooperation of commercial firms to produce plasma fractions, priority should be given to establishing fractionation plants as part of national transfusion services ... The establishment of such a plant in a national service acts as an incentive to improve the service because it has control of its plasma and is able to prepare those fractions that are needed.

In January 1976, Dr Perrault submitted to the national commissioner of the Red Cross a summary of the steps that had been undertaken to evaluate the establishment of a national fractionation plant within the blood transfusion service. Dr Perrault said that the project should be considered urgent. The need for urgency was explicitly identified as the pressure from Connaught for a five-year fractionation contract.

At its regular annual meeting on 9 April 1976, with Dr Watt's final report before it, the scientific advisory committee of the blood transfusion service reiterated the recommendation made at its extraordinary meeting in December 1975 – that the Red Cross establish its own fractionation plant. This recommendation was not based on the quality of Connaught's blood products, which the committee found to be "excellent," but on three other factors: Connaught did not possess a modern full-scale fractionation plant; it had low yields; and it did not produce fractions for which there was low demand.

Connaught's control over these factors was limited. Improvement of its plant was held up while the Red Cross delayed committing itself to providing an adequate supply of fresh frozen plasma. Low yields of factor IX concentrate, in turn, were the result of that obsolete plant and the quality of the plasma (stored, not fresh frozen) supplied by the Red Cross. As to the third factor, Dr Perrault testified at the Inquiry that it is difficult to meet the demand for "niche" products from voluntary donations.

Relying upon the report of Dr Watt, the repeated recommendation of the blood transfusion service's scientific advisory committee, and the statements of the World Health Organization and the League of Red Cross Societies, Dr Perrault asked the sub-executive committee of the Red Cross to seek federal support for a Red Cross fractionation plant. On 9 May 1976, the committee agreed to do so.

The chair of the Red Cross's executive committee wrote to the Minister of National Health and Welfare, Marc Lalonde, on 24 June, proposing that the Red Cross build a fractionation plant. In describing the then current situation, he contrasted the not-for-profit fractionation of voluntarily donated plasma with the for-profit fractionation of plasma from paid persons, citing the World Health Organization, the League of Red Cross Societies, and the International Society of Blood Transfusion as having urged the development of the former and having "universally condemned" the latter. This contrast was inaccurate to the extent that it related to the Connaught–Red Cross relationship. Connaught's intention as a for-profit fractionator was to process the Red Cross's voluntarily donated plasma, not plasma given for money. Moreover, the statements by the international organizations had not condemned that type of relationship. They expressed a preference for not-for-profit fractionation, but recognized that it might "be necessary to enlist the cooperation of commercial firms to produce plasma fractions."

Mr Lalonde responded to the Red Cross by letter on 24 September 1976. He set out three governing principles for the blood supply system: protection of the system of voluntary donation; national self-sufficiency in blood products; and gratuity of blood products to recipients. These three principles were endorsed by the Red Cross four days later and by representatives of the provinces on 23 November. Mr Lalonde also stated that, while the Red Cross proposal appeared "to meet these principles and to offer significant advantages to the Canadian health care system," he could not commit the provinces to the proposed project, and some form of intergovernmental consultation would be required. He said he had already written to his provincial counterparts, and hoped he could soon convene a meeting at which the Red Cross could make a presentation.

That meeting, attended by provincial and federal officials, was held on 23 November 1976. Dr Perrault presented the Red Cross proposal. On 17 December, Mr Lalonde told the Red Cross that the governments were granting it \$150,000 to prepare a study to support the proposal, and that they would consider ways in which the project might be financed if it were approved. From this time through 1981, when the provinces jointly decided who should be Canada's domestic fractionators, decisions about fractionation grew increasingly more political than scientific.

Connaught–Red Cross relations

In developing its factor VIII concentrate, Connaught had assumed that the Red Cross would supply the fresh frozen plasma to make it and that the Red Cross would distribute the resulting product, both for clinical trials and eventually for general use. In June 1976, the same month it approached the federal government for support for its own fractionation plant, the Red Cross for the first time told Connaught expressly that it would not supply Connaught with fresh frozen plasma.

By late 1976, Connaught was licensed to conduct clinical trials of its factor VIII concentrate and had enrolled several Canadian physicians who treated hemophiliacs to carry them out. Those physicians, like Connaught, assumed that Connaught's product, both in the trials and later for general use, would be distributed free of charge by the Red Cross. In a memorandum to file dated 13 December 1976, Dr Perrault identified the Rh Institute–Connaught relationship as a threat to a Red Cross fractionation plant. In late 1976, the physicians who were to conduct the trials learned that the Red Cross would not distribute Connaught's product for the trials or for general use. The physicians began to withdraw from the trials.

Connaught held a meeting with the hemophilia-treating physicians on 28 January 1977, and Dr Perrault attended. Dr Martin Inwood, one of the nation's leading hemophilia-treating physicians, argued that to participate in the trials would serve no purpose. Without fresh frozen plasma from the Red Cross, Connaught's product would never be available in quantities

sufficient for general domestic distribution, and that, in his view, could make participation in the trials unethical. The Rh Institute could not produce sufficient plasma for large-scale production of factor VIII concentrate. The risk that hemophiliacs will develop adverse side-effects increases with the number of concentrate products they use. It is therefore understandable that physicians would not want to increase that risk by having their patients use a product for a clinical trial if there was no likelihood that it would become generally available.

Two days later, the executive of the Canadian Hemophilia Society met with its medical and scientific advisory committee. The society is a not-for-profit organization, founded in 1953 and incorporated in 1977, whose purpose is to assist hemophiliacs through education, research, and the promotion of the best possible treatment of hemophilia. In 1977, its advisory committee included several of the physicians who were to participate in the trials. After the meeting, the society and the members of its advisory committee jointly asked all physicians to withdraw from the trials. Their reasons were, first, that the product involved was made from plasma for which donors had been paid, a situation that would "probably lead to the collapse of the volunteer blood donor collection system in Canada," and, second, that the Red Cross would soon be distributing factor VIII concentrate made from plasma from Red Cross volunteer donors. The minutes of the meeting record two sources of information leading to that conclusion. One was a memorandum by Dr Inwood describing the meeting between Connaught and the physicians of 28 January, and the other was a presentation by Dr Perrault as a member of the medical and scientific advisory committee. In fact, Connaught was using plasma from donors paid by the Rh Institute only because it could not get plasma donated by volunteer donors from the Red Cross for its clinical trials. Moreover, Connaught wanted any factor VIII concentrate it produced for general distribution to come from plasma derived from Red Cross volunteer donations. The Red Cross was thus in control of both aspects of the situation.

The domestic clinical trials collapsed, but Connaught completed the clinical trials of its factor VIII concentrate through three physicians in the United States. Although delayed, licences were eventually granted by both the Health Protection Branch of the Department of National Health and Welfare and the U.S. Food and Drug Administration.

During this same period, 1975 and 1976, stories critical of Connaught appeared in the *Globe and Mail*, the CBC-TV program *The Fifth Estate*, and *Maclean's* magazine. The negative publicity was serious for an organization undergoing the change from not-for-profit to profit-making status; it affected morale within the organization, already weakened by the sale of Connaught by the University of Toronto. At the same time, it strengthened the resolve of the senior management to remain in the fractionation business, since leaving might be seen as an admission of incompetence. The stories published and

broadcast were based in part on statements made by Red Cross officials. These statements were perceived by Connaught's senior managers as part of a concerted plan to force Connaught out of the fractionation business in order to enhance the prospects for the Red Cross's own fractionation proposal.

Throughout 1976, both Connaught and the Red Cross lobbied governments to support their plans. Both corporations tended to exaggerate. Connaught minimized the problems with Building 50 and the resources needed to renovate it to current standards. The Red Cross overstated the seriousness of the problems with the quality and yield of Connaught's products. The conflict became so openly hostile that Pierre Gravelle, a federal assistant deputy minister of health and welfare, brought the two parties together on 16 May 1977. At that meeting, it was agreed by all that, although lobbying of the governments would continue, there would be no further public statements by either organization to strengthen its position and, if problems that needed resolution arose, Mr Gravelle would again convene a meeting of the two sides.

The Ad Hoc Federal-Provincial Committee on Plasma Fractionation

In March 1977, the federal and provincial deputy ministers of health created the Ad Hoc Federal-Provincial Committee on Plasma Fractionation, with representatives from the federal and provincial governments. It was the first of three government committees that would address the question. The purpose of this group (commonly referred to as the Ad Hoc Committee) was to review the Red Cross fractionation proposal, study other fractionation options, develop short-term arrangements for the provision of blood products, and recommend long-term measures "to ensure a continuous and adequate supply of blood product requirements in the future."

The Ad Hoc Committee first met in July 1977. It received submissions from Connaught in January and June 1978. The Red Cross relied upon its November 1976 fractionation proposal and submitted a supplementary submission in June 1978. The committee presented an interim report to the deputy ministers on 10 November 1978, but required additional financial information from potential domestic fractionators other than the Red Cross before making its final report, which it did on 2 February 1979.

In its first brief, Connaught described the past relations between Connaught and the Red Cross, its own capabilities, its view of the consequences that would result from its disappearance as a fractionator, and its idea of how the system should operate. The review of past relations was essentially a recital of complaints about the Red Cross, particularly the quality of its plasma and its impediments to Connaught's development of factor VIII concentrate. Connaught evaluated its own abilities favourably. It submitted that its existing fractionation plant had been modernized to current industry

standards; that it was constantly reviewing improvements to existing fractionation technology and alternative processes; and that it was capable of expanding its fractionation plant within a short period to make Canada self-sufficient in therapeutic blood products. The claims about its plant were exaggerated. Subsequent reports by Connaught and the Bureau of Biologics on Building 50, in 1979 and 1980, still described it as "antiquated" and "badly in need of modernization and upgrading."

The Connaught brief warned that failure to fund its proposal would have the following serious consequences:

- An estimated annual increase of \$2,224,000 will have to be levied on all remaining Connaught products, should Connaught cease plasma fractionation.
- A capital writeoff of \$1,100,000 and a lay-off of a minimum of 49 staff will result if Connaught has to close its fractionation plant.
- Setting up of a BTS [blood transfusion service] plant will be regarded by private industry as a "nationalization" as funds will have to be provided by Government and [Connaught's] plant is already existing.
- The establishment of a BTS plant will have a serious deleterious effect on attracting pharmaceutical research and production to Canada.

Connaught proposed a ten-year partnership with the Red Cross, in which the Red Cross would concentrate on increasing the quantity and quality of its fresh frozen plasma while Connaught concentrated on fractionation. That Connaught would propose linking itself to an organization with which it had such an acrimonious relationship reflects the strength of its desire to remain the nation's domestic fractionator. Connaught also said that without any further outlay of capital it could immediately fractionate more plasma than it was currently doing, and that, at a cost of \$3.4 million, its plant could be expanded within eighteen months to meet all domestic blood product demand through 1986. These claims might have been excessive, but they were never put to the test.

The Red Cross's supplementary submission included a commissioned engineering study that provided cost estimates for its proposed plant. They were approximately \$20.5 million to build and start up a fractionation plant capable of processing 150,000 litres of plasma per year, and approximately \$1.6 million more to expand the capacity of the plant to 300,000 litres. The engineers considered the proposal financially practical and predicted that, at the then current price of fractionated products, the cost of the plant could be recovered from sales in six years. The Red Cross made three principal arguments before the committee: Canada's domestic fractionator should be not for profit; the Red Cross was the best candidate to operate a not-for-profit fractionation plant because the integration in one enterprise of plasma

collection, fractionation, and distribution of blood products would be most efficient and effective; the Red Cross was also the best candidate because it had provided detailed plans showing how it could build a plant and pay for it within six years, and enable it, as a not-for-profit corporation, to provide products at much lower cost than any commercial operation could.

There is no direct way of knowing whether this final argument was justified. The Red Cross claim was based on the engineering study by Surveyer, Nenniger & Chenevert Inc. (SNC Inc.), which, in turn, was based on a study by financial consultants Galasco Consultants Ltd. (Galasco). Galasco approached the Ad Hoc Committee directly to express concerns about the way in which its study had been interpreted:

We disagree with SNC Inc.'s interpretation of our Market, Marketing and Resource Study. Our Financial Analysis is excluded from the SNC Inc. report. The content and conclusion of the SNC Inc. and Galasco Consultants Ltd. Financial Analysis are substantially different.

When the engineering firm was invited to appear with the financial consultants to assist the committee in understanding the financing of the proposed fractionation plant, one of its vice-presidents responded:

I would like to inform you that we are readily available to discuss at your convenience with you or with your committee any of your concerns relating to our report on plasma fractionation. May we, on the other hand, point out that we do not believe it proper for us to attend a meeting where you have deemed it necessary to invite one of our sub-consultants who are directly and legally responsible to us.

For your information, our attorneys are taking the pertinent procedures against Galasco for unethical practices.

The committee was then, and I am now, deprived of knowing the basis of this dispute.

Much of the debate that followed related to the for-profit versus not-for-profit issue. Connaught, in its second brief to the committee, proposed to charge prices for fractionated products that would "reflect its total production and capital cost, and include a margin similar to that accepted by the Federal Government on contracts issued by DSS [the Department of Supply and Services] under their costing memorandum." In other words, Connaught proposed to take a fixed profit above costs, an approach that would shield it from losses because all costs would be covered, but one that would prevent unacceptably high profits because the profit margin would be fixed.

The Red Cross, on the other hand, based its proposal on the “preservation and development of the volunteer system” and presented for-profit fractionation as a threat to that principle:

The transfer of [Connaught] to the private sector placed the Red Cross in the position of answering one million volunteer blood donors as to why profit should be made on their gift. And this question is being asked more and more frequently, both nationally (T.V., Press) and internationally.

The submission reviewed the inherent dangers of, and experiences in other countries with, paid plasmapheresis and the international plasma trade, and warned that paid plasmapheresis would be a consequence if the system of voluntary donation faltered:

In the above context, it can be understood that the concept of voluntarism in blood must be preserved where it exists, expanded where it does not meet the country's goals, and developed where it does not exist. The insertion of any country, developed or otherwise, in the vicious circle of an uncoordinated or non-existent national blood system at the mercy of the pressures of commercial plasma operations represents a triple danger:

- high costs;
- increased medical risks; and
- constant threat of public opinion outcry, if the country becomes a source of paid plasma exports or if the country has an existing volunteer donor base and feels its base is threatened by commercialism.

The brief concluded with the submission that a total national approach to the supply of blood and plasma fractions must be considered “to preserve the volunteer system; to collect the right proportion of whole blood and plasma to meet national needs; and to be free of the international pressure of the plasma trade.”

The Ad Hoc Committee reported its findings and made eight recommendations in its interim and final reports to the deputy ministers. It said that current arrangements for supplying the Canadian health care system with blood products fell short of ensuring that all needs were met. The status quo, the committee found, was “inherently unstable” and “not consistent with the three principles advocated by the Ministers of Health” – voluntary donation, self-sufficiency, and gratuity. The sources of instability and inconsistency were several: concerns about the Red Cross’s ability to manage its blood transfusion service; Connaught’s inability to supply all therapeutic blood products; the fractious Connaught–Red Cross relationship, which was seen

as "not conducive to ensuring adequate blood products for the future"; the importation of significant quantities of blood products (made from plasma from persons who were paid) because of domestic insufficiency; excess fractionation capacity worldwide that was vulnerable to collapse; changing technologies; and increasing demand for products. The following, in brief, are five recommendations that appeared in both of the reports:

- a national blood policy should be developed to define standards "for blood product utilization, for information on all aspects of the blood product market, and [to] ensure Canada's blood resources are managed efficiently";
- the Rh Institute, being an important organization in the supply of immune globulins and in experimentation with new fractionation techniques, should become affiliated with the national fractionation plant;
- as the preferred short-term solution to guaranteeing adequate supply in a cost-efficient way, the Red Cross should use open-bid tendering to choose a fractionator for its fresh frozen plasma; at the same time, Connaught and the Red Cross should enter into a formal contract for the fractionation of stored plasma;
- a board should be created, composed of Red Cross, federal, and provincial officials, supported by scientific and financial advisory committees, to oversee the blood transfusion service and fractionation services, to ensure that national blood policy would be followed and that the services would be responsive to user needs, and to provide policy guidelines to the services;
- the federal government should underwrite 50 per cent of the capital costs of building or improving a fractionation plant that would be operated on a not-for-profit basis.

In the principal recommendation – the choice of Canada's domestic fractionator – the final report stated:

The majority of the Committee recommend that, on the basis of economics, effective organization of the national blood services, and the principles enunciated by the Ministers of Health, that one 200,000 litre fractionation plant be established, to be owned and operated by the Canadian Red Cross Society, under the supervision of the board of management previously recommended by this committee.

Three provincial representatives, supporting local interests, dissented from the principal recommendation of the final report. Each came from a province that was home to a manufacturer that had put forward a fractionation proposal: the Rh Institute in Manitoba, Connaught in Ontario, and the Institut Armand-Frappier (Armand-Frappier), a not-for-profit corporation making biological products located near Montreal and associated with the Université du Québec.

The report of the Ad Hoc Committee was considered at a conference of deputy ministers of health in Ottawa on 6–7 March 1979. The deputy ministers formed a new committee, the Ad Hoc Committee on Canadian Policy on Blood and Blood Products, and accepted three of the old committee's recommendations: that a national blood policy be developed; that the Rh Institute be affiliated with the national fractionation plant; and that blood products used for diagnostic tests be treated differently than blood products used in medical treatment. They did not agree with the Ad Hoc Committee's principal recommendation – that a Red Cross fractionation plant be built. The minutes record that the deputy minister of health of Ontario said his province "could not support any change from the present production facilities on the basis of present information." Quebec's deputy minister "asserted that blood plasma fractionation was a part of provincial responsibility in the health field, considered that the committee had exceeded its mandate, and criticized federal intrusion in the health sector." He went on to say that Quebec would establish its own fractionation plant. The deputy ministers decided to suspend consideration of identifying a national fractionator and of methods of financing a not-for-profit plant until the new committee had reported. That committee consisted of representatives from Alberta and the three dissenting provinces – Ontario, Quebec, and Manitoba – and had a reporting date in late 1980. Alberta's deputy minister, G.J. Chatfield, chaired the committee, which then became known as the Chatfield Committee.

The Red Cross voiced strong disagreement with the deputy ministers' decision. It wrote directly to all eleven ministers of health, reiterating the view that commercial fractionation was a threat to the principle of voluntary donation, protesting that the delay in reaching a decision would have "the deliberate effect of killing the Red Cross proposal," and asserting that "this course of action not only prevents the integrated operation of a National Blood Transfusion Service, but is a clear impediment to its continued orderly operation. Indeed, it may be a threat to the continuation of a National Blood Service."

The Chatfield Committee

The Chatfield Committee was given the tasks of developing long-term solutions to the fractionation problem and supervising short-term contractual relations in order to ensure security of supply. At its first meeting, on 22 May 1979, the committee decided to develop a long-term Canadian policy for blood and blood products to be proposed to the ministers of health conference in December 1980. It defined the short-term issues before it as

- (a) the one-year contract for fresh frozen plasma and stored plasma;
- (b) the establishment of contractual arrangements between the Red Cross and Connaught, so that long-term policy options remain open to the Ministers of Health; and

- (c) the policy implications of the three principles endorsed by the Conference of Deputy Ministers of Health.

Between the time of the decision of the deputy ministers in early March 1979 and the time of the meeting of the committee in May 1979, the Red Cross had negotiated fractionation contracts that threatened to foreclose some of the long-term policy options.

The domestic supply of blood components had increased substantially since Connaught was refused fresh frozen plasma. By October 1977, the Red Cross had determined that it would be able to deliver 50,000 litres of fresh frozen plasma for fractionation over the next year, and in that month it signed its first contract for that purpose – with a U.S. commercial fractionator, the Hyland Products Division of Travenol Laboratories International (Hyland). The Red Cross subsequently supplied Hyland with fresh frozen plasma to manufacture factor VIII concentrate, factor IX concentrate, and albumin. Connaught continued to fractionate the Red Cross's stored plasma, manufacturing blood products other than factor VIII concentrate.

The last shipment of fresh frozen plasma to Hyland under the 1977 contract was scheduled for 25 April 1979. On 14 March 1979, the Red Cross requested tenders from Connaught and two U.S. fractionators, Hyland and Cutter Laboratories Inc. (Cutter), for the fractionation of its next 75,000 litres of fresh frozen plasma. On the same day, it requested tenders from the same three manufacturers for the fractionation of 70,000 litres of stored plasma. On the basis of price, the Red Cross chose Cutter for both contracts.

The Red Cross knew that awarding Cutter the contract to process stored plasma would have the effect of ending Connaught's business as a fractionator, and that the decision might have political implications. Dr Perrault, in recommending the award, wrote in a memorandum to the national commissioner of the Red Cross:

Processing [the stored] plasma in the United States, in addition to the F.F.P. [fresh frozen plasma], has the effect of taking all Canadian Red Cross plasma away from Connaught. It is expected that this will cause some problem with Connaught. However, the Cutter price is substantially lower and their offer is attractive. In order to minimize disruption, Cutter have agreed not to begin the fractionation of [stored] plasma before October 1st, 1979. This would enable a formal four-month notice to be given to Connaught on June 1st, that fractionation of Canadian Red Cross plasma in their laboratories would cease ...

Should any political repercussions arise from this transaction, Cutter have indicated they are quite prepared to deal with them.

On 27 April 1979, the Red Cross informed Mr Chatfield that it had already signed the fresh frozen plasma contract with Cutter and was planning to sign the stored plasma contract with Cutter on 1 June. Dr Perrault had recommended the delay in signing the second contract to give the Chatfield Committee time to communicate any objections.

There were indeed objections. The first came from Connaught. The Red Cross had told Connaught on 9 May that it would no longer be the Red Cross's fractionator of stored plasma, but offered to delay the change until 30 September. Dr William Cochrane, Connaught's chair and chief executive officer, responded:

The decision of the Red Cross, as you will appreciate, now places a very major issue before not only the Company but other constituencies in Canada. For the Company the consequences are the discontinuance after October of a major operation, with considerable financial loss and more importantly the likely termination of up to fifty employees. Of greater significance and importance is the loss of Canadian technological expertise for a considerable period of time by, at present, the only company in Canada that is capable of providing a degree of self-sufficiency in blood fractionation products for the Canadian people. As a result this places the provision of blood fractionation products for Canadians in the hands of companies outside this country.

While your decision is most disappointing to us, I must admit that for myself it does not come as a total surprise. In light of our recent meeting and discussions that were held, I felt that a clear strategy position had been taken by the Red Cross Society that would likely seriously affect Connaught Laboratories.

Dr Cochrane went on to say that, since there appeared to be no further opportunity to discuss the matter with the Red Cross, Connaught could "only look forward to discussions" with the Chatfield Committee.

The committee discussed the matter on 22 May. Dr Cochrane reported that Connaught had decided to remain in the fractionation business and was considering several options for doing so. These choices included seeking an embargo on the export of Red Cross plasma, buying American plasma to make products for export, and developing a paid plasmapheresis operation. Dr Perrault and Dr Alvin Zipursky, chair of the blood transfusion service advisory committee, made the Red Cross's presentation. They did not find a friendly reception. There was open disagreement over the Red Cross's use of tenders for the fractionation contracts. The committee noted that the deputy ministers had considered but not endorsed this method of awarding contracts after it had been recommended by the Ad Hoc Committee. The representatives of the Red Cross said their organization disagreed with the deputy

ministers. The Chatfield Committee pointed out that awarding the stored plasma contract to Cutter through an invited tender had serious implications. It threatened national self-sufficiency, gave Connaught cause to develop a paid plasmapheresis operation, had serious financial consequences for Connaught and others, and precluded options otherwise open to the ministers of health. The committee asked the Red Cross to reconsider its decision, and the Red Cross agreed to do so. On 19 June, the committee asked the Red Cross to seek an extension from Cutter to 30 October for signing the stored plasma contract, so that the ministers of health could consider the matter at a conference scheduled for September. They also asked Connaught to refrain from developing a paid plasmapheresis operation until 30 October.

On 19 July 1979, the committee formulated a short-term (three- to five-year) recommendation and long-term options. The short-term recommendation was for Connaught and the Red Cross to enter into contracts under which Connaught would continue to fractionate all the Red Cross's stored plasma and would gradually, over the course of three years, become the fractionator of all the Red Cross's fresh frozen plasma. The committee set out five alternative long-term options. In the first three, fractionation would be carried out by one of the Red Cross, Connaught, or Armand-Frappier, and in the fourth, by a combination of domestic fractionators. All these recommendations assumed that the Red Cross would continue to collect donations and to distribute blood products. The fifth option was for "provincial acquisition and distribution of blood and blood products." The committee was unable to decide a fundamental issue that needed to be resolved before it could choose from among the five long-term options – whether domestic fractionators of Red Cross plasma should be allowed to earn profits from their operations. That question was referred to the ministers.

In September 1979, the committee reported to the ministers of health as follows:

The current status of the Canadian blood and blood product system is unstable and untenable in the absence of long-term policy commitments by the provincial and federal governments. The current situation is characterized by:

- (a) an increasing reliance on foreign owned fractionators;
- (b) a continuing unstable and antagonistic relationship between the National Blood Transfusion Service and Connaught Laboratories;
- (c) a potential development of commercial paid plasmapheresis with its unknown effects [that] may pose a possible threat to voluntary donor system in terms of quantities and costs of collections; and
- (d) a less than cost effective blood and blood product system.

The committee recommended that the ministers reaffirm the three principles of voluntary donation, self-sufficiency, and gratuity as the foundation of the Canadian blood supply system. Because it was thought that the advent of paid plasmapheresis seemed likely and might have a negative impact on the voluntary donor system, it recommended that "the individual provinces take the appropriate steps to prohibit the development of profit-oriented paid plasmapheresis operations." It concluded that for-profit fractionation, although contrary to the position of the Red Cross that "no profit should be made from blood," was not contrary to any of the three principles, and that, since all the fractionators with which the Red Cross was dealing were for-profit corporations, Connaught should not be excluded for that reason from consideration for a short-term contract. The committee therefore recommended that the federal and provincial ministers of health should not, in the short term, "restrict the operations of profit-oriented firms within the [fractionation phase] of the Canadian blood and blood product system." It then added a long-term recommendation against for-profit fractionation:

However, the Committee recommends, in the long term, that only non-profit operations be permitted within the processing component. In order to not exclude Connaught Laboratories, the Committee recommends that the federal government review and consider changing Connaught's corporate status and its present profit motivated objectives.

The committee then made more specific recommendations. For the short term, it recommended that Connaught and the Red Cross enter into a one-year contract containing the following conditions:

- Connaught would continue to fractionate Red Cross stored plasma;
- in addition to the stored plasma, Connaught would receive fresh frozen plasma from the Red Cross for a total (including Rh Institute plasma) of 90,000 litres of plasma per year;
- yields and deliveries would be determined by Connaught and the Red Cross but would have to be approved by the Chatfield Committee;
- additional costs (beyond the price available through open bidding) would not exceed \$1,160,000;
- Connaught would agree to fractionate for the full contractual period and would agree not to develop a paid plasmapheresis operation during that period.

Quebec officials later told the Red Cross that their province had dissented from the recommendation for a one-year contract, but this disagreement is not recorded in the report. The committee reported, finally, that it could not recommend, for the long term, a domestic fractionator until the ministers had resolved the issues set out earlier in the report.

Provincial responses

The ministers of health met on 17 September 1979. The minutes of the meeting record that, after some initial inconclusive discussion about long-term options, Mr Chatfield asked the ministers at least to deal with the recommendation for the one-year contract. Quebec's Minister of Health, Dr Denis Lazure, "recommended that purchases from Connaught Laboratories be encouraged on the condition that the price offered by Connaught be comparable to current prices." The ministers knew that Dr Lazure's condition could not be met because the Chatfield Committee had reported that, in the first year alone, the cost of using Connaught to fractionate the Red Cross's stored plasma would be approximately \$1 million more than the Cutter bid. Ontario's Minister of Health, Dennis Timbrell, said, according to the minutes,

that the approach suggested by Mr Lazure would mean that raw materials would be shipped to Cutter in the U.S.A. to fractionate, as American operators can undercut Canadian operations due to excess capacity in the U.S. He suggested that it is worth paying the necessary price to ensure Canadian self-sufficiency.

After some discussion of the three principles, Dr Lazure responded: "To suggest that a contract be given to Connaught regardless of price is not acceptable to Quebec. Quebec does not intend to give a grant to the Red Cross to buy blood products at above-market prices." After once again endorsing the three principles, the ministers, Dr Lazure dissenting, decided that, "in the short run, a contract should be arranged between the Red Cross and Connaught Laboratories for stored plasma."

Immediately after the ministers' conference, pressure was put on the Red Cross by both Ontario and Quebec. On 18 September, the day after the ministers met, Dr Perrault received a telephone call from Dr Allen Dyer, an assistant deputy minister of health for Ontario and the province's representative on the Chatfield Committee. According to Dr Perrault's memorandum to file, Dr Dyer told him that "if the fractionation 'principles' were not adhered to in blood, Ontario would consider going it alone." Dr Perrault assumed that the "principles" referred to were the terms of the one-year contract that the ministers had endorsed. Six days later, the two men met. According again to a memorandum to file written by Dr Perrault, he reviewed the costs of operating the blood transfusion service in Ontario and the benefits that the province received from the service, and said it was for the province to decide whether it wanted to operate its own service. He recorded that Dr Dyer, at the end of the meeting, said that Ontario "did not really want to run its own transfusion service but that they certainly wish their interests to be protected."

Roger Ladouceur, executive assistant to Dr Lazure and an occasional representative to the Chatfield Committee, also called Dr Perrault on 18 September

He invited Dr Perrault to attend a meeting with Quebec's deputy minister, Jean-Claude Deschesnes, to discuss fractionation. That meeting took place on 25 September. I infer from the documentary evidence setting out Quebec's position at the time that Mr Deschesnes told Dr Perrault that Quebec would not, under any circumstances, pay an amount for blood products that was above the market price as defined by the Cutter bid.

The positions of Ontario and Quebec created a dilemma for the Red Cross. In order to maintain adequate supplies of blood products, it had to enter into a contract for fractionation of its stored plasma. By entering into a contract with either Connaught or Cutter, it would probably incur the displeasure of one or other of Canada's two most populous provinces. Instead, the Red Cross decided not to enter into any contract until it had a written decision from "an authoritative source," and communicated this decision to Donald MacNaught, chair of the Federal-Provincial Program and Budget Review Committee, the committee that then reviewed and approved the blood transfusion service's annual budgets:

Based ... on the assumption that we will, in fact, be asked to enter into a contract with Connaught Laboratories, we are prepared to begin negotiations of a one-year contract with them for the fractionation of stored plasma derived from our Transfusion Service, provided we receive the assurance that costs so incurred over the present tender offer from Cutter Laboratories will be covered through our existing funding mechanism.

The Red Cross, in effect, left it to the provinces to decide who would pay any additional costs.

The problem was not resolved by the end of October 1979, and the Red Cross obtained a further one-month extension from Cutter. The situation later became more complicated. In November, Quebec told the Red Cross that it was withdrawing from the Federal-Provincial Program and Budget Review Committee. That committee was therefore no longer a body to which the Red Cross could look for authoritative national decisions.

Connaught and the Red Cross engaged in contract negotiations as stipulated by the ministers of health. On 12 December 1979, they agreed that the contract should be for 47,000 litres of stored plasma and 17,000 litres of fresh frozen plasma. For the first time, Connaught would receive from the Red Cross fresh frozen plasma as the raw material for its newly licensed factor VIII concentrate.

A joint-venture proposal for fractionation

During this difficult period the Red Cross never lost sight of the goal of its own fractionation plant. In 1979, it proposed engaging in a joint venture with a private fractionator, an approach it hoped might overcome any objection to

its proposal based on its lack of experience in the field. The Red Cross initially considered only foreign fractionators as potential partners. Nothing came of these approaches.

The possibility of a joint venture with a domestic fractionator was eventually broached, and at the ministers' conference on 17 September 1979 it was agreed that the Minister of National Health and Welfare, David Crombie, would assist Connaught and the Red Cross to develop such a plan. In doing so, however, he was expected to consult with the provinces and other possible partners, including the Rh Institute and Armand-Frappier.

No dissent is recorded in the minutes of the conference, but on 4 October Mr MacNaught learned that Quebec did not regard the federal minister as authorized to negotiate a joint venture on its behalf. He was told that Quebec would be investigating its own joint venture with the Red Cross. Indeed, in the Red Cross–Quebec meeting of 25 September, the deputy minister, Mr Deschesnes, had already raised the possibility of joint development of a Quebec-based fractionation plant by the Red Cross, Armand-Frappier, and the province. This proposal never came to fruition.

On 22 February 1980, Dr Perrault sent a joint-venture proposal to Dr Cochrane at Connaught. The joint venture was to be not for profit and controlled by a board of directors to consist of federal, provincial, Connaught, and Red Cross representatives, with the Red Cross having "the privilege of the chair and the majority of votes." Connaught and Red Cross officials met to discuss the proposal, and on 8 April Dr Cochrane gave Connaught's formal response. Although Connaught looked forward to further discussions, it had several concerns about the proposal: excessive bureaucracy in the governing structure; the delegation of Connaught's decision-making authority; and the fact that the Red Cross had a majority on the board and held the position of chair. Dr Cochrane suggested as an alternative a national blood and fractionation advisory committee, operating for two years on a trial basis and supported by the federal and provincial governments, the Red Cross, Connaught, and other domestic fractionators. He proposed that such a committee would make suggestions that participants in the blood system could respond to voluntarily. His proposal was not accepted.

Later fractionation contracts

While the choice of a domestic fractionator was being debated, the Red Cross had to procure an adequate supply of blood products. It did so in two ways. First, it imported factor VIII concentrate bought from the American Red Cross. The need to import concentrate reflected the fact that Canada then, like most countries even today, could not meet domestic demand for blood products solely from voluntary blood donations. The imported concentrate was made by Hyland from the fresh frozen plasma of American Red Cross volunteer donors. Second, the Red Cross signed a new contract with Cutter for the fractionation of Canadian fresh frozen plasma. That action precipitated a crisis.

The original Cutter contract to fractionate fresh frozen plasma for the Red Cross was to expire in the spring of 1980. On 14 March 1980, the Red Cross requested tenders from Connaught, Cutter, and Hyland for the fractionation of 55,000 litres of fresh frozen plasma during the remainder of 1980, 90,000 litres in 1981, and 100,000 litres in 1982. On 4 May, the Red Cross awarded the contract to Cutter, whose bid was 32 per cent lower than that of its nearest competitor. The decision was communicated on 8 May to Mr MacNaught, with a request that the Federal-Provincial Program and Budget Review Committee approve the contract by 28 May. On 28 May, Mr MacNaught asked Dr Perrault to delay signing the contract until 6 June "to permit sufficient time for Mr Chatfield to complete consultation with all provinces." Unlike the Federal-Provincial Program and Budget Review Committee, the Chatfield Committee (which had the mandate to supervise fractionation contracts) still had a representative from Quebec. On 6 June, Mr MacNaught reported to Dr Perrault by telexed message:

The chairman of the ad hoc [Chatfield] committee of deputy ministers on blood and blood products has advised that the consensus of the provinces is to accept the tender of Cutter Laboratories. Therefore, I am authorized by Mr Chatfield to advise the Red Cross Society to proceed with the contract with Cutter Laboratories for 245,000 litres of fresh frozen plasma for the period ending December 1982.

On 9 June, the Red Cross entered into the contract with Cutter. Dr Perrault recommended that the contract be signed even though Ontario, Nova Scotia, and British Columbia were opposed to it. He predicted at that time that Ontario would "express its displeasure"; the provincial reaction was delayed, but it was as he had expected.

On 5 September, Red Cross officials met with several Ontario officials at the province's request. The Red Cross memorandum of the meeting records that it was chaired by an assistant deputy minister of industry and tourism, D.M. Allan, who referred to the signing of the Cutter contract as "stupidly irresponsible." He again raised the possibility of Ontario's withdrawing from the Red Cross blood program. The Red Cross officials asked for a formal written statement of the provincial position, which was immediately forthcoming:

We ask you to undertake the following remedial actions:

- 1) Cancel the Cutter contract at the earliest possible date.
- 2) Re-direct the plasma raw material committed under the Cutter contract to Connaught Laboratories to process these essential products in Canada.
- 3) Work with the provinces and Connaught Laboratories to fully utilize Canadian capacity for blood fractionation with the objective of meeting total Canadian needs at the earliest possible date ...

As we stated, there is a critical urgency to this matter. We look forward to an initial response by 10:00 a.m. September 8, 1980.

The Red Cross needed consistent instructions. Dr Perrault had become ill on 26 June and was unavailable to deal with this crisis. Dr B.P.L. Moore, acting national director of the blood transfusion service in Dr Perrault's absence, decided to refer the entire matter back to the Chatfield Committee for resolution. However, in a new telexed message, Mr MacNaught repudiated any implication that he or the federal government had authorized the Cutter contract in its message of 6 June and suggested that sending the matter back to the Chatfield Committee would be ineffective:

Neither the Federal-Provincial Program and Budget Review Committee nor the federal government per se authorized the Red Cross to proceed with the Cutter contract.

The Chairman of the Ad Hoc [Chatfield] Committee of Deputy Ministers on Blood and Blood Products, whose mandate was to expedite the development of contractual relationships between suppliers and manufacturers of blood and blood products, canvassed all provinces in May and early June 1980 and advised me on June 6, 1980 that the consensus of the provinces and federal government was to accept the tender of Cutter Laboratories Limited. This authorization was communicated to you via my telex of June 6, 1980.

The current dispute between the Red Cross and Ontario arises because Ontario does not agree with the majority consensus of the provinces.

I would recommend that the Canadian Red Cross Society contact all provinces and the federal government by telex or letter at the earliest opportunity outlining the problem, and the implications for the security and cost of blood products supply that would result from the actions proposed by assistant deputy ministers of the ministries of industry and tourism and health of the government of Ontario.

I recommend that the Red Cross contact all health ministers prior to the forthcoming meeting of ministers of health, tentatively scheduled for September 29 in Winnipeg.

The Red Cross was still considering its position when, on 11 September, the situation became public. Ontario's letter to the Red Cross demanding cancellation of the Cutter contract was leaked to the media. Mr Timbrell and Dr Cochrane then held a press conference. Mr Timbrell said that the Cutter contract endangered security of Canadian supply because blood products manufactured by Cutter might be embargoed by U.S. authorities in an emergency. He said that it also threatened the availability of free blood products and the development of Connaught's fractionation program. He contended

that it was worth paying the additional \$5 million the concentrate would cost if Connaught were awarded the contract. Dr Cochrane said that he felt that Cutter was using "predatory pricing" (submitting an artificially low bid to force Connaught out of business), and that the problem arose because the Red Cross wanted to build its own fractionation plant despite the existence of Connaught's. He estimated that fifty positions would be lost if Connaught stopped fractionating.

The same day, Mr Timbrell asked Red Cross officials to meet in his office. Henri Tellier, the national commissioner, Dr John Derrick, director of operational research, and Dr Ian Morgan, national director of administration, attended for the Red Cross; the provincial representatives included Mr Timbrell and the Minister of Industry and Tourism, Larry Grossman, as well as six members of their staffs. The Red Cross memorandum of the meeting records that Mr Timbrell expressed concern about the leakage of the letter but proposed that, since the information now was with the media, "it appeared as if the two bodies should try to keep this matter as low key as possible without it becoming an emotional issue of settling differences in the media." Dr Dyer said that, as Ontario's representative on the Chatfield Committee in May and June, he had understood Mr Chatfield to be taking a poll of positions on the Cutter contract and had not understood him to be taking a formal vote authorizing the signing of the contract with Cutter. He went on to question what authority the Red Cross had to sign a contract that Ontario was known to oppose. The deputy minister of health, Tom Campbell, said that

as long as he had been in the ministry, Red Cross had taken the attitude of disregarding the wishes and opinions of the province almost to the point of insulting the province, and that, with the number of dollars the Province of Ontario contributes to the Blood Transfusion Service, the volume of blood Ontario donors put into the system and the amount of products utilized by Ontario hospitals, [the Red Cross] should pay much greater attention to the Ontario position, and ... suggested that, in any situation where the province of Ontario dissents from a majority decision, the Red Cross should then negotiate two positions: one for the others; one for Ontario.

Mr Allan added that

it was incredible for anybody to believe that the CRCS [Red Cross] had acted in good faith in negotiating the Cutter contract and to him it was clearly evident that the Red Cross had no intention of supporting Connaught and had gone out of their way to obtain the contract with Cutter Laboratories.

The Red Cross was in an impossible position. Ontario clearly viewed itself as entitled to a veto over any decision made by the Red Cross or the other provinces that affected Ontario. At the same time Quebec, by refusing to pay any additional costs for a Connaught contract, was in effect claiming a counter-veto.

A meeting took place four days later between Mr Campbell and Dr Dyer, for Ontario, and the Red Cross's committee on fractionation, but it did not resolve the impasse. At that meeting, the Red Cross took the position that it had obligations to all eleven ministers of health and asked Ontario to respect its need to reach a "well-considered decision based on the wishes of all concerned." Mr Campbell and Dr Dyer said this position "was unacceptable to Ontario," and raised the possibility of legislation to protect Connaught's interests.

Despite Mr Timbrell's request for a low-key approach, both Connaught and the Red Cross issued press releases attacking each other. The last of these releases was issued only two days before the ministers of health, including the federal Minister Monique Bégin, were to meet on 29 September.

The Chapin Key Report

The ministers from Ontario, Quebec, and Manitoba advanced the interests of their local manufacturers at the meeting on 29 September. Then Mr Timbrell made a suggestion that received a positive reply from Dr Lazure:

MR. TIMBRELL: I have no difficulty, absolutely no difficulty with Frappier and Connaught and the Rh Institute being competitive amongst themselves. That's fine because it's all Canadian and it's going to stay all Canadian. That's fine with me. Where I have difficulty is that, as I said earlier, what we've got now is the situation where the blood and the bucks are going offshore and the effect can only be to destroy the Canadian industry, which could have been rebuilt in some manner of means in two and a half to three years' time. Inasmuch as Connaught has already indicated its willingness to become a regulated utility, I think we should pursue that and provide and allow for and encourage development of Canadian alternatives perhaps. If that's the wish of the Government of Quebec, that's fine. Let's have competition within Canada.

DR LAZURE: Madame la Présidente, à ce que je sache, le Québec est encore dans le Canada. Armand-Frappier est dans le Canada ...

MME BÉGIN: Dennis [Timbrell], I understood you to speak to being competitive within Canada. Doesn't that mean you are suggesting two plants?

MR. TIMBRELL: I'm saying that if Quebec goes ahead, as it has the right to do, to develop the capacity of Armand-Frappier, that's their decision and

eventually what we'll have is competition between Connaught, which is publicly owned, which is willing to be a publicly regulated utility, and Frappier, and perhaps even the Rh Institute as well. And that's fine.

Mr Timbrell then suggested that, if there was agreement to develop the domestic industry and if the Cutter contract was antithetical to that development, the provinces should form a "users' group" to determine how to extricate the Red Cross from its obligations to the Cutter contract. The ministers recognized that developing competitive domestic fractionators, given the limited Canadian demand, could lead to higher prices because all three plants would be small scale. Dr Lazure said Quebec nevertheless was willing to consider Mr Timbrell's proposal. Mme Bégin suggested that various options, including the Red Cross proposal, could be reviewed by the deputy ministers, who were to meet in November. The provincial ministers were meeting without Mme Bégin the next day, however, and Mr Timbrell suggested that they spend some time then establishing the users' group. Mme Bégin objected to that proposal because the federal government's interests would not be represented. Mr Timbrell made it clear that Ontario might not wait until November, in view of the importance of the matter to his province. Mme Bégin closed the discussion by stating again that the matter would go to the deputy ministers and then come back to the ministers, but there was no agreement that that was the best way to deal with the issue.

The next day, the provincial ministers agreed to form a users' group of representatives from Nova Scotia, Saskatchewan, Newfoundland, and British Columbia with the mandate

to examine and recommend in regard to the capital, operating and technical feasibility of producing blood fractionation products by one or more of the three plants operated by or proposed to be operated by Connaught Laboratories, Rh Institute and Armand Frappier, keeping in mind the three principles affirmed by the Ministers of Health.

The users' group, formally known as the 1980 Inter-Provincial Ad Hoc Committee on Plasma Fractionation, was chaired by Dr Chapin Key, British Columbia's deputy minister of health, and its report became known as the Chapin Key Report. Its terms of reference effectively eliminated any consideration of the Red Cross proposal.

Mr Timbrell and his deputy met with the chair of the Red Cross executive committee, W.R. Livingston, on 3 November. Mr Timbrell reported that the provincial ministers of health had decided to consider only the three fractionation plants. Ontario's position, he said, was that all Ontario plasma should be fractionated domestically, which for the time being meant by Connaught, because it was the only licensed domestic fractionator.

The Chapin Key Report was transmitted to the provincial ministers of health on 24 November 1980, less than two months after the committee was formed. The committee admitted that it had not had the time to verify all the facts, but felt that it was in a position to make the following recommendations:

- the ministers of health should establish an "Authority on Blood Policy" in order to eliminate the uncertainty existing within the system;
- to ensure security of supply, at least two domestic fractionation plants should be developed;
- fractionation of plasma for domestic consumption should be not for profit, but fractionation for foreign consumption could be for profit. If "any laboratory is unable or unwilling to accept this principle, steps should be taken to ensure non-profit prices to the provinces through subsidies or other actions by the host province";
- the Cutter contract should be renegotiated;
- Connaught should receive 70,000 to 90,000 litres of plasma per year for the next three years to allow development;
- expansion and modernization of a 100,000-litre Connaught plant should be approved, provided Connaught agreed that its fractionation operation would be not for profit;
- any loss of profit by Connaught should be a matter of discussion between it and the Province of Ontario;
- subject to the approval of Quebec, Armand-Frappier should be authorized to establish a 100,000-litre not-for-profit plant;
- the Rh Institute should be designated for specialized fractionation of immune globulins;
- the Rh Institute should be associated with one of the other fractionators to facilitate the development of new technologies, such as column fractionation, and for marketing and distribution;
- only 50 per cent of development and capital costs for the fractionation plants should be recoverable from the prices charged to all provinces for blood products, it being assumed that the home provinces of the fractionators would be willing to assist by providing the other 50 per cent;
- the Red Cross should continue to be responsible for the collection, primary processing, and distribution of blood and blood products.

When the ministers of health of the provinces and territories next met, in Toronto on 15–16 December, Manitoba's Minister, Louis Sherman, said his province could not support the recommendation for only two plants, with the Rh Institute in a subordinate role. He was supported by Alberta's Minister, David Russell, who argued that there should be a plant in western Canada. Dr Lazure then proposed that the development of three plants be approved, with Armand-Frappier to take only 50,000 litres rather than 100,000, leaving Connaught with 100,000 litres and giving the Rh Institute 50,000, the national

total remaining the same. Both Mr Timbrell and Dr Lazure vehemently opposed a suggestion that the Red Cross proposal be re-examined. The provincial ministers of health accepted the recommendations of the Chapin Key Report as amended by Dr Lazure's suggestion. They announced that three Canadian non-profit locations were to be considered "on economic, security of supply, and regional grounds, especially in light of new technological developments in the fractionation field."

The ministers asked the committee to provide an addendum to its report, because of the change from two to three domestic fractionators. That addendum, delivered on 11 June 1981, recommended that, in the long term, once all three fractionation plants were operating, 50 per cent of all Canadian plasma collected for fractionation should be sent to Connaught Laboratories, with the other 50 per cent shared equally between the Institut Armand-Frappier and the Rh Institute. With regard to renegotiation of the Cutter contract, the committee reported that Ontario had agreed to be completely responsible for certain related costs; these costs included any damages payable to Cutter, any increase in the cost of factor concentrates to the end of 1982, and 50 per cent of capital and development costs and all taxes incurred by Connaught.

By this time, given the political decisions that had been made, the Red Cross had begun planning new fractionation contracts. In late March 1981, in accordance with those decisions, it decided to request a tender from Connaught for a three-year contract, to run to the end of 1983, for the fractionation of both fresh frozen plasma (a total of 105,000 litres over the three years) and stored plasma (also 105,000 litres over the three years). At the same time, it decided to ask Cutter to agree to amendments to the existing, controversial contract. That contract, which was scheduled to run to the end of 1982, was to be extended by one year. While the total amount of fresh frozen plasma to be supplied for fractionation to Cutter over the term of the contract remained the same because of the one-year extension, the amount to be fractionated by it each year decreased, providing a supply for Connaught to fractionate. Ontario found this course of action acceptable. At the same time, the Red Cross sought written assurance that Ontario would indemnify it for additional costs incurred through these contracts. Written assurances were given, both directly by Ontario and indirectly through the Federal-Provincial Program and Budget Review Committee, but they were not as detailed as the Red Cross would have liked. The Red Cross eventually entered into negotiations with both Connaught and Cutter, but continued to ask for clarification of the assurances it had already received.

The new contractual terms were proposed to the fractionators on 1 June 1981. Ontario, being financially interested because of its assurances to the Red Cross, was an observer to the Cutter-Red Cross negotiations, which were successfully concluded. Cutter agreed to the one-year extension on 22 September, and the Federal-Provincial Program and Budget Review Committee ratified it in November. The negotiations with Connaught were much more

complicated. They involved the Red Cross, Connaught, Ontario, the Federal-Provincial Program and Budget Review Committee, and its successor, the Canadian Blood Committee. They were complicated by confusion over the additional costs related to Connaught's fractionation program that Ontario was willing to bear, an issue that had to await the next meeting of the provincial ministers of health at the end of September before it could be resolved. Even then, ten more months passed before the Connaught-Red Cross contract, covering the period January 1981-December 1983, was finally signed in mid-summer 1982.

Under the terms of this contract, Connaught was to recover its costs and, in lieu of profit, receive \$775,000 for research. At the same time, a second contract between Ontario and Connaught gave Connaught a further \$1,225,000 during the course of the Connaught-Red Cross contract, contingent on Connaught spending at least \$10.5 million for research during that time and entering into the first contract. There was no provision for profit in either of these contracts. However, through them Connaught received \$2 million in research money during three years when its net profit was approximately \$11.3 million.

The consequences of conflict

Connaught's proposal, that it develop modern processes and improve Building 50 so it would be able to provide Canada with a full range of therapeutic blood products, depended upon agreement by the Red Cross to deliver the plasma of Canadian donors. The Red Cross, to enhance the prospects for its own proposal, withheld the plasma and thwarted Connaught's plans.

The Red Cross's proposal, to create a fully integrated blood transfusion service that included a modern fractionation plant, was dependent on approval by the provinces. Ontario was concerned to advance Connaught's interests and, although it was unable to persuade other provinces to adopt Connaught as the nation's only fractionator, it thwarted the plans of the Red Cross to build its own fractionation plant.

Both proposals were reasonable, and either one had the potential to make Canada self-sufficient in fractionation capacity, but they were mutually inconsistent. Despite the attempt to find common ground, Connaught and the Red Cross failed to create an alternative proposal that was mutually acceptable.

With both proposals rejected, the provincial governments ultimately decided to divide the available plasma. Each of the three provinces that was home to a manufacturer with fractionation aspirations secured for that manufacturer an assured share of the Red Cross plasma. That compromise might have been politically satisfying in the short term, but in the long term it meant that no single manufacturer was assured a sufficient volume of plasma to make its fractionation operations financially practical.

In the end, Connaught did not undertake the necessary renovation of Building 50, the Rh Institute did not distribute a licensed factor concentrate, and Armand-Frappier did not build a fractionation plant. As a result, although Connaught produced blood products until 1988, Canada remained dependent on U.S. fractionators for a full supply of blood products throughout the 1980s. The decline of the domestic fractionation industry is discussed in Chapter 17.

5

The Canadian Blood Committee and Its Relationship with the Canadian Red Cross Society

The Canadian Blood Committee, the funder of the blood program in the 1980s, was a recent creation. Its first meeting was held in December 1981 and it did not become fully operational until the middle of 1982, when its secretariat came into existence. By then, the Canadian Red Cross Society (Red Cross) had operated the Canadian blood system for several decades.

This chapter describes the process by which the Canadian Blood Committee was created by the provincial ministers of health and its structure, organization, and powers. It discusses the often difficult relationship between the Canadian Blood Committee and the Red Cross during the 1980s, when the two organizations should have been working together to implement measures to protect the safety of the blood supply.

The tensions that developed between the Red Cross and the Canadian Blood Committee were related in part to the Red Cross's adherence to the seven fundamental principles that guide the international Red Cross and Red Crescent movement. One of these is that every national society be independent of government. When the blood program began in 1947, it was not difficult for the Red Cross to maintain its independence. At that time, the program was financed by the Red Cross alone. As the blood program grew, however, and as it became a more integral and important part of the provincial health care systems, government assumed an increasingly high proportion of the cost. With the increasing financial commitment came an increasing need, in the view of the provinces, for supervision and control of the expenditure of taxpayers' money.

The relationship between provincial governments and the Red Cross

The Canadian Blood Committee was created to enable the provinces to exercise control over and to oversee the blood system. The peculiar organization of the committee, which is described below, arose out of the peculiar nature of the blood program in Canada and its relationship with the health care system.

The *Constitution Act, 1867*, reserves to either the federal Parliament or the provincial legislatures the subject matters in which each has exclusive jurisdiction to enact laws. Health is not one of the enumerated subject matters and therefore is not within the exclusive legislative jurisdiction of either the federal Parliament or the provincial legislatures. Rather, both are given legislative authority touching upon matters of health. The federal Parliament has the power to legislate in respect of international and interprovincial trade and commerce, criminal law, and the residual power in matters of peace, order, and good government. The power to legislate in respect of criminal law is very broad and extends to safeguarding the health of the public against harmful and injurious effects. It allows the federal Parliament to enact legislation to protect persons from potential harm from products, whether they be pesticides, vitamins, cigarettes, or drugs. Parliament also has exclusive legislative jurisdiction with respect to marine hospitals, aboriginal health matters, and the provision of health services to military personnel. Provincial legislatures have powers over local matters, hospitals, and property and civil rights. In practice, most health services in Canada are administered and paid for by the provinces, with the assistance of substantial grants from the federal government.

The blood program was a national program in a provincial system. It was administered by the national office of the Red Cross, but it was paid for by the provinces. Most decisions that the Red Cross made about the blood program had a financial impact on every provincial government. The entire budget of the Red Cross's blood transfusion service and 80 per cent of the budget of its blood donor recruitment program were paid for by the provinces. In any decision that had financial implications, the Red Cross therefore had to deal with ten governments.

The period from 1971 to 1981 was one of discord in the Canadian blood system. During this time there was conflict between the Red Cross, which operated the blood system, Connaught Laboratories Limited (Connaught), which manufactured blood products, and the provincial governments, which funded the blood system. Much of the controversy, which is described in greater detail in Chapter 4, was about the manufacture and supply of fractionated blood products. The Red Cross had been supplying Connaught with plasma since 1947, and Connaught had used that plasma to produce fractionated products for distribution by the Red Cross. By 1972, Connaught's plant and processes were outmoded. Connaught began the process of improving or replacing its facilities and aspired to be a modern manufacturer of blood products. By 1975, however, the Red Cross also had aspirations to manufacture blood products. Dr Roger Perrault, who had become the national director of the blood transfusion service in the previous year, wanted the Red Cross to be able to meet Canada's need for blood and blood products independently, through a comprehensive program beginning with the collection of blood components and ending with the supply of blood components and

manufactured plasma derivatives. Throughout the mid-1970s, both Connaught and the Red Cross sought government support for their respective plans for fractionation plants and sometimes fought their battles in the media. The relationship between the two organizations, which had been close and cooperative, became increasingly hostile – and the future of the Canadian blood system became increasingly uncertain.

During the next several years, a number of government committees were struck to attempt to mediate the dispute. By this time, two other organizations, the Winnipeg Rh Institute Inc. of Manitoba and the Institut Armand-Frappier of Quebec, had proposed that they too become fractionators of Canadian plasma. In 1977, the federal and provincial ministers of health created the Ad Hoc Federal-Provincial Committee on Plasma Fractionation. This committee released its final report in 1979. The majority of its members recommended that the Red Cross own and operate a fractionation plant. The three representatives from Ontario, Quebec, and Manitoba dissented. The committee reported to the deputy ministers in March 1979. The recommendation for a Red Cross fractionation plant was not accepted and a new committee, chaired by Mr G.J. Chatfield, was created. This was the Ad Hoc Committee on Canadian Policy on Blood and Blood Products, which became known as the Chatfield Committee.

The Chatfield Committee reported in September 1979 with short-term recommendations for immediate implementation and a number of long-term proposals. One of the proposals was for the formulation of a national blood policy. It did not answer the question who should be the fractionator of Canadian plasma. Before the committee reported, the Red Cross had awarded a contract for the processing of fresh frozen plasma to Cutter Laboratories Inc. (Cutter), a U.S. fractionator, in preference to Connaught, whose bid had been much higher. This became a sensitive political issue in which senior provincial officials, including the Minister of Health of Ontario, became involved. The contract caused conflict between the Red Cross and some of the provinces and also conflict among the provinces themselves, in particular between Ontario, which supported Connaught, and Quebec, which favoured Cutter's lower bid.

A third and smaller committee, the 1980 Inter-Provincial Ad Hoc Committee on Plasma Fractionation, of which Dr Chapin Key was the chair (thus, the Chapin Key Committee), recommended in November 1980 that there be two fractionators in Canada – Connaught and the Institut Armand-Frappier. The ministers of health accepted this recommendation in the following month, and at the same time decided that the Winnipeg Rh Institute should be designated as a third Canadian fractionator.

Their decision effectively brought to a close the fractionation dispute of the 1970s. After several years of conflict among the Red Cross, Connaught, and several provincial governments, the Red Cross's hope of owning and operating its own fractionation plant was ended.

Recommendation for the creation of a Canadian blood authority

The Chapin Key Committee concluded that one of the reasons for the dispute over fractionation in 1979 and 1980 was the lack of a clear "authority" supervising the blood program. In the absence of such an authority, it was unclear who should make decisions regarding the blood program, and as a result the Red Cross, the provincial governments, and Connaught were often in conflict. The committee was also aware that there was in Canada no counterpart to the Food and Drug Administration in the United States that regulated the collection, processing, and supply of blood components.

The committee recommended that the ministers appoint a group to establish the structure and mandate of a Canadian authority to oversee the blood program:

The absence of an authority to develop a structure around the principles concerning blood resources and to develop consensus among the groups concerned with the supply and utilization of these resources is a reason why so much uncertainty exists in Canada at this time. In this regard, the 1980 [Chapin Key] Committee has confirmed the observations of previous Committees that some Canadian Authority be created to oversee the blood program, and to develop the principles and resolve the other issues raised herein. Although the 1980 Committee had not had sufficient time to develop concrete plans in this regard, it is strongly recommended:

THAT THE MINISTERS ACT IMMEDIATELY TO APPOINT REPRESENTATIVES TO A GROUP DELEGATED TO ESTABLISHING THE STRUCTURE AND MANDATE OF A CANADIAN AUTHORITY, USING AS A BASIS THE RECOMMENDATIONS AND SUGGESTED TERMS OF REFERENCE ENUNCIATED IN THIS REPORT.

The committee proposed terms of reference for the authority. After revision in January 1981, these were as follows:

1. To establish policies with regard to the following:
 - a) the collection of blood, including plasmapheresis
 - b) the processing of blood
 - c) the distribution of blood products
 - d) the utilization of blood products
 - e) operational research in the areas of blood or blood products.
2. To allocate resources to meet costs of implementing these policies.
3. To assure adherence to established policies by the Canadian Red Cross, plasma fractionation plants, and others involved in the collection, processing, distribution, and utilization of blood and blood products.
4. To establish policy and recommend on the export and import of human blood and blood products.

5. In the short term, to adjudicate that fractionation plants are being developed according to the recommendations of provincial, and territorial Ministers, and to reallocate resources and priorities, if necessary, to ensure their implementation.
6. To assure that standards are developed to aid in implementation of policies.

The committee proposed that the authority consist of a board of representatives from all the provinces and the federal government and carry out some of the tasks of governments. It would create broad policy guidelines, allocate funding, and ensure compliance with standards. It would not, however, operate or manage the blood system. One of its primary responsibilities would be to approve budgets and audit expenditures. Sufficient resources would be made available for it to carry out its duties properly. Support staff with financial expertise would be needed, as would a technical advisory committee, independent of the Red Cross, because the provincial representatives could not be expected to have expertise in blood. The committee believed that there would have to be a formal delegation of financial jurisdiction over the blood system from the provinces to the new authority. The authority would also be "quasi-regulatory" in the sense that it would ensure that standards of blood and fractionated blood products were met. It would interact not only with the Red Cross, but also with any fractionators manufacturing blood products for use in Canada.

After it reported in November 1980, the Chapin Key Committee was asked to recommend the structure and mandate of the proposed blood authority. Its preferred approach was to create a not-for-profit corporation, to which the federal and provincial governments would delegate their authority, and which would have the ability to enter into contracts with the Red Cross. The Chapin Key Committee described the structure and powers of a central authority of this type in a report that was presented to the federal-provincial ministers of health at a meeting on 30 September and 1 October 1981.

The provinces that were to have fractionation plants (Ontario, Quebec, and Manitoba) opposed the creation of an independent authority. The ministers of health decided that they were not prepared to create a separate legal entity with the power to approve budgets that the provinces would be required to honour. They did, however, agree to create a federal and provincial committee that would carry out some of the objects proposed for the authority. This was an approach the Chapin Key Committee had considered and rejected for the following reasons:

This option would not allow sufficient independence to advise and direct without much consultation with superiors, which would tend to make it less responsive than corporate decision-making. It would lack authority to

deal with the issues in an effective manner. Technical input and involvement of non-government agencies would be distant from the final decision-makers ... [A] permanent federal-provincial secretariat would be cumbersome to establish and maintain.

The creation of the Canadian Blood Committee

The Canadian Blood Committee was created in the autumn of 1981 after the conference of ministers of health. Its first meeting was held on 3 December 1981. Mr Ambrose Hearn, the deputy minister of health of Newfoundland, was elected the chair. A draft of the committee's terms of reference was distributed to the members. These terms of reference, largely drawn from those drafted by the Chapin Key Committee, were as follows:

Purpose

To direct the Canadian blood system in accordance with the principles established by the Ministers of Health for the therapeutic use of human blood, blood products or their substitutes.

Objectives

1. To establish policies with regard to the following:
 - a) the collection of blood, including plasmapheresis;
 - b) the processing of blood;
 - c) the distribution of blood products;
 - d) the utilization of blood products;
 - e) operational research; and
 - f) support and maintenance of the four enunciated principles concerning blood and blood products.
2. To recommend allocation of resources to meet costs of implementing the above policies.
3. To assure adherence to established policies by the Canadian Red Cross, plasma fractionation plants, and others involved in the collection, processing, distribution, and utilization of blood and blood products.
4. To consult with the Department of Industry, Trade and Commerce on appropriate policies for the export and import of human blood and blood products.
5. To consult with the Bureau of Biologics, Department of National Health and Welfare, on appropriate policies for the regulatory control of the collection, processing, and distribution of blood, blood products and their substitutes.
6. In the short term, to monitor the development of fractionation plants to ensure that their establishment is in accordance with the recommendations of the Ministers of Health and allocate resources and priorities for their implementation.

7. To determine the real costs of producing blood fractions for Canadians and the shareable portion of capital costs to be added to the price of blood fractions.
8. To ensure that standards for blood, blood products and blood substitutes are developed, and to monitor that such standards are met.
9. To review and approve the programs and budgets of the Blood Donor Recruitment and Blood Transfusion Services of the Canadian Red Cross Society, subject to the concurrence of all Provinces and Territories.
10. To report annually to the Ministers of Health on all activities of the Committee.
11. To be a national forum for the various organizations and associations of the Canadian blood program to discuss issues, and to coordinate the activities related to the management of the Canadian blood system.

As conceived, the Canadian Blood Committee was to have representatives from every provincial and territorial government and the federal government. In practice, although the territories were members of the committee, they never sent representatives to the meetings. The government of Quebec originally sent no representative but was kept informed through the committee's minutes; beginning in December 1982 it sent an observer to the meetings, but it did not formally join the committee until October 1983. Although the federal government did not directly pay a share of the costs of the blood program, it was a full participant. The federal government paid the salaries of the members of the secretariat, who were federal government employees.

The committee did not have independent power to decide matters that involved substantial amounts of money. It had no independent budget, no line of credit, and no power to enter into contracts. It could not bind a provincial government that dissented from a decision of the representatives of the other provinces. The committee therefore had to attempt to seek consensus and to be unanimous in its decisions. Only rarely did it put a matter to a formal vote. Occasionally, individual provinces opted out of particular aspects of the blood program or made separate arrangements with the Red Cross.

Decisions about the budget of the Red Cross were delayed because every member of the committee had to seek the approval of his or her government for its portion of the expenditures. All members of the committee were employees of the ministries or departments of health of their provinces, most coming from the division that established budgets for hospital and ambulance services. Their expertise was in accounting or financial management. Only a few had a medical or scientific background.

Membership on the Canadian Blood Committee was never a representative's primary duty within his or her ministry or department of health. The business of the committee took, on average, no more than 5 to 10 per cent of a member's time and required his or her attendance at approximately four meetings per year.

At its first meeting, the Canadian Blood Committee created a structure for itself. It appointed an executive committee, consisting of the chair and representatives of Ontario, western Canada, Atlantic Canada, and the federal government. A representative of Quebec was added later. The executive committee was intended to facilitate the work of the full committee and, between meetings of the full committee, to make decisions on its behalf that were not sufficiently important to require the consideration of all the members. The first task of the executive committee was the creation of a secretariat.

The Red Cross response to the Canadian Blood Committee's terms of reference

After the first meeting of the Canadian Blood Committee, Mr Hearn sent a copy of its draft terms of reference to Dr Perrault, who had attended a portion of the meeting as a guest. Mr Hearn asked the Red Cross to advise the committee about the nature of the technical and scientific subcommittee that should be established. Dr Perrault expressed the views of the Red Cross in a letter to Mr Hearn dated 20 January 1982:

The draft terms of reference of your Committee, although similar to those generally outlined in the [Chapin] Key Report of December 1980, have caused some concern in the Canadian Red Cross Society, as it seems to be the will of the Provincial Ministers of Health to proceed with the Canadian Blood Committee [CBC], and its terms of reference, without the benefit of an established National Blood Policy to govern the CBC.

You will recall that in 1978, the Federal-Provincial Ad Hoc Committee on Plasma Fractionation submitted its report to the Conference of Deputy Ministers of Health, recommending with a majority vote that the Canadian Red Cross build a plasma fractionation facility. In March 1979, the Deputy Ministers did not accept that recommendation, citing the lack of a National Blood Policy. To correct this, the Chatfield Committee was established, with the added mandate of preparing short-term recommendations for the negotiation of plasma fractionation contracts.

The Chatfield Committee never reported on part of its mandate, i.e. a proposal for a National Blood Policy. The Key Committee was formed to resolve the difficulties of the plasma fractionation issue, and in its report recommended the formation of a "Canadian Blood Authority." The recommendation seemed to be based mainly on the issue of the "dispute" of fractionation (see page 47 of Key Report). From this recommendation, the Canadian Blood Committee was formed on 30 September 1981. In November 1981, we wrote to you expressing our desire to see the terms of reference of the Committee.

Having reviewed these draft terms of reference, our National Executive Committee has serious concerns about the lack of a National Blood Policy, and the broad and far-reaching terms of reference of the CBC. We wish

to inform you of our general concerns at this time and would like to offer our assistance and collaboration to the CBC in addressing some of these concerns and perhaps assist you in the process of defining a National Blood Policy. It would appear to us that the Canadian Blood Committee's terms of reference could then be re-examined in a better light. We have already begun detailed work on the question, and will forward to you a detailed document in March 1982.

Mr Hearn responded to Dr Perrault on 1 February 1982. He said that he did not agree that the recommendation for a blood authority was based mainly on the dispute over fractionation. He pointed out that, in making its recommendation, the Chapin Key Committee, of which he had been a member, had reviewed not only fractionation but also the collection, processing, and distribution of blood and blood products. With respect to the terms of reference, he wrote that

[t]he terms of reference of the Canadian Blood Committee are broad, but, by necessity, they must be so to enable the Committee to fulfil the mandate set for it by the Ministers of Health. As one part of its mandate, the Canadian Blood Committee is required to make recommendations to individual Ministers of Health with respect to a budget for the Red Cross Blood Transfusion Service and other programs relating to blood and blood products that the Red Cross undertakes on behalf of Health Departments in Canada.

The Canadian Blood Committee looks forward to receiving from the Red Cross its detailed comments on the terms of reference of the Committee in March, 1982, and to working with the Red Cross to resolve issues of mutual concern.

The Canadian Blood Committee did not wait for the Red Cross's comments. At its next meeting, on 3 February 1982, only two days after the date of Mr Hearn's letter, the committee approved its terms of reference.

The Red Cross completed a "commentary" on the terms of reference on 12 April 1982. It was a lengthy document that, among other matters, expressed concern about the term of reference authorizing the Canadian Blood Committee to "direct" the Canadian blood system. The Red Cross urged that its independence should "be maintained through government *support* rather than *direction*" (emphasis in the original). The commentary again stressed the importance of the creation of a national blood policy, within which the Red Cross could operate but still retain its autonomy.

The Red Cross's commentary was not well received. Dr Perrault was told that one member of the Canadian Blood Committee had called it a "pile of crap" and that other members had said that the Red Cross was a poor manager that

now was telling others how to manage. At a meeting on 17 June 1982 the Canadian Blood Committee, without any extensive discussion, decided not to amend the terms of reference.

The secretariat

By April 1982, the committee had hired an executive director for its secretariat. Dr Denise Leclerc-Chevalier, whose academic background was in pharmacy and hospital management, had been the director of the bureau of drug quality, part of the Health Protection Branch of the Department of National Health and Welfare.

The secretariat was intended to provide the committee with an office and services, including administration, research, and the distribution of written materials to members. Its principal task was to review the budget submissions of the Red Cross and to make recommendations about the budget to the committee.

The executive director was expected to be aware of information affecting the Canadian blood system that could be gathered from sources such as governments, industry, scientific journals, or the Red Cross, so that she could in turn keep members of the committee informed. She was, in short, given the task of being the committee's eyes and ears. In order to carry out this task, she communicated with organizations both inside and outside Canada, including the Red Cross, the Bureau of Biologics (the federal regulatory body), the Council of Europe, and the World Health Organization. Her role was especially important because of the lack of expertise of most members of the committee in technical and scientific issues concerning blood. The executive director also sat on a number of advisory committees, including that of the Red Cross blood transfusion service and, after it was established in 1983, the National Advisory Committee on AIDS.

The secretariat was small and overworked. In addition to the executive director, it consisted of a financial analyst, a program analyst, and a secretary. It was housed within the Department of National Health and Welfare. Although the executive director was a full-time servant of the committee, she regularly prepared briefing notes for the Minister of National Health and Welfare and reported to an assistant deputy minister in that department who was a member of the Canadian Blood Committee.

The advisory subcommittee

Soon after the Canadian Blood Committee was formed, it began the process of creating a technical and scientific subcommittee, eventually known as the advisory subcommittee, that could provide the expertise required for it to make informed decisions about the blood program.

The committee considered two options for selecting the membership of the subcommittee at its meeting on 3 February 1982. The first option was to form a subcommittee of experts in the various aspects of the blood system. The second option was to form one of representatives of various organizations that were interested in the blood system, among them the Red Cross, the Canadian Medical Association, the Bureau of Biologics, and the Canadian Cancer Society. It was recognized that representatives of some of these organizations might not personally have expertise in blood issues. This lack could be overcome, however, by the use of working groups or task forces that would include persons with specific expertise appropriate to the task.

At its next meeting, on 4 March, the committee chose the second approach and decided to invite representatives from organizations including the Red Cross, the Canadian Hemophilia Society, and the Canadian Medical Association. Representatives were also invited from the three Canadian fractionators – Connaught Laboratories Limited, the Winnipeg Rh Institute Inc., and the Institut Armand-Frappier. No representatives from U.S. fractionators were invited, even though Cutter by this time was the largest supplier of factor concentrates to the Canadian market. The terms of reference drafted for the advisory subcommittee were:

To provide advice to the Canadian Blood Committee on matters relating to the blood system in Canada, including:

- a) standards for blood, blood products and substitutes and policies to maintain and improve these standards;
- b) new technologies, or new uses for existing technologies, affecting the blood system, e.g. plasmapheresis;
- c) operational research in the blood area; and
- d) any matter referred to it by the Canadian Blood Committee.

In its commentary on the Canadian Blood Committee's terms of reference, the Red Cross expressed its views about the type of advisory body that should be created and the role it should play. The Red Cross was concerned that the composition of the new subcommittee might turn out to be "virtually identical" to that of the advisory committee of its own national blood transfusion service, which was made up of experts in matters related to blood transfusion. If that were to happen, it said, committee members, with two masters, would face potential conflicts of interest. It suggested different means of providing the Canadian Blood Committee with advice. One suggestion was to appoint a representative of the Canadian Blood Committee to the Red Cross's advisory committee. Another was to form an advisory subcommittee that would include representatives from user groups, medical associations, and professional groups and that would provide "a forum for discussion of matters of common or shared interest in addition to those of [a] strict technical and scientific nature."

The first meeting of the advisory subcommittee was held on 25 August 1982. In attendance were representatives of the Red Cross, the Canadian Medical Association, the Canadian Hospital Association, the Canadian Hemophilia Society, the Canadian Association of Pathologists, the Canadian Cancer Society, and the three Canadian fractionators. Dr Perrault attended as the representative of the Red Cross. Of all the members of the subcommittee, he had the greatest expertise in all aspects of the blood system. In the months and years that followed, the other members deferred to his views on the issues of blood collection and blood banking. The Bureau of Biologics, the regulator of the blood system, had sought to be represented, but the committee decided that the bureau should communicate with it through the secretariat. Eventually, however, the bureau did take part in the advisory subcommittee, first as an invited guest in April 1984, then as an observer in October 1984, and finally as a member from November 1985.

At its first meeting, the advisory subcommittee considered the terms of reference that had been drafted for it by the Canadian Blood Committee. The members interpreted their role in narrower terms than those drafted; they believed that there should be no duplication between the roles of the Canadian Blood Committee and the Red Cross, or between those of their own advisory subcommittee and either the Bureau of Biologics or the advisory committee of the Red Cross blood transfusion service. They did not believe that they were knowledgeable enough to give advice on appropriate standards of quality for blood, new technologies, operational research, or other technical matters as proposed in the draft terms. Rather, they saw the subcommittee acting as a "forum for discussion" and a liaison among all parties involved in the Canadian blood system – the role suggested by the Red Cross in its commentary.

The Canadian Blood Committee knew how its advisory subcommittee interpreted its function. Dr Leclerc-Chevalier was present at the subcommittee's first meeting, as was Dr Donald Ingraham, New Brunswick's representative on the Canadian Blood Committee, who was the chair of the advisory subcommittee. Dr Ingraham reported the advisory subcommittee's interpretation of its role to the full committee. The advisory subcommittee was never told that its interpretation was inappropriate or too narrow.

The advisory subcommittee only infrequently gave advice to the Canadian Blood Committee. It met, normally, only twice a year. It did not create any specialized subcommittees or task forces to assist it. The Canadian Blood Committee rarely referred matters to it for advice. From time to time, however, the advisory subcommittee decided on its own to advise the committee, as, for example, in October 1984 when it resolved that the Canadian Blood Committee call a "consensus conference" to determine whether there should be a conversion to heat-treated factor concentrate.

A national blood policy

For some time before the creation of the Canadian Blood Committee, it was apparent that an express national policy regarding the blood system would clarify the roles and relationship of the Red Cross and governments. The Red Cross had long sought such a policy. Governments had been less forthcoming, but in 1976 the Minister of National Health and Welfare, Marc Lalonde, wrote to the Red Cross setting out three governing principles for the blood supply system. They were:

- (i) protection of the system of voluntary donation
- (ii) national self-sufficiency in blood and blood products
- (iii) gratuity of blood products to recipients.

In 1979, the Chatfield Committee considered whether domestic fractionators should be allowed to make a profit from the manufacture of concentrates from plasma collected by the Red Cross from voluntary donors. It recommended that domestic fractionation should be non-profit in the long term but that, since the U.S. fractionators with which the Red Cross had dealings were all profit-making corporations, the federal and provincial governments should not in the short term restrict the operations of profit-oriented Canadian fractionators (that is, of Connaught). The ministers of health endorsed the three principles and, with Quebec dissenting, agreed to a short-term solution for domestic supply through Connaught. The desirability of non-profit domestic fractionation subsequently came to be recognized as a fourth guiding principle.

The Canadian Blood Committee had been given the task of establishing policies with regard to the blood program as the first of its terms of reference, and the Red Cross, from its earliest communications with the committee, had stressed the importance of a national blood policy. When the advisory subcommittee met in December 1982, it resolved that it should draft the policy. The committee rejected its subcommittee's resolution and said that it would itself draft a national blood policy after consultation with other parties. The Red Cross was a member of the advisory subcommittee, but not of the full committee. The reasons for the committee's decision are set out in the minutes of its meeting in December 1982, and were as follows:

Members of the CBC recognized the need and the urgency of developing such a policy, as approved by the Conference of Ministers of Health. However, they did not agree to give the Red Cross the responsibility to prepare the working document because it might be perceived as being biased. The Committee also decided to keep the leadership in this activity. Consequently all consultation will be done by the CBC.

In March 1983, the committee decided that the following elements should be included in a national blood policy:

- the four principles enunciated by the Ministers of Health;
- the terms of reference of the Canadian Blood Committee and its authority;
- the applicability of the policy to:
 - the Canadian Red Cross Society;
 - the fractionation and related industry;
 - all governments;
- the role and corporate principles of the Canadian Red Cross Society and its contractual relationship with governments and hospitals;
- international provisions;
- authority for product standards development, implementation and control;
- authority for policy decisions, implementation, monitoring and appeal;
- recognition of blood as a public, national and limited resource;
- research and development.

Under the supervision and direction of the committee, the secretariat took on the task of drafting the policy and predicted, in June 1983, that the policy would be published by 1985.

The secretariat invited more than fifty groups, including the Red Cross, to work with it in developing the national blood policy. By the summer of 1985, a "sensitizing text" had been prepared and sent to all parties involved. The Red Cross submitted draft documents to the secretariat in the autumn and winter of 1986-7. In June 1987, the secretariat completed a first draft of the policy, which it sent to forty organizations for comment; thirty-two of them replied. A second draft, completed in February 1988, was sent to the same organizations; twenty of them replied.

In February 1989, some members of the Canadian Blood Committee concluded that the original principles approved by the ministers of health in 1979, and upon which the draft policies had been based, needed further review and that the ministers should be asked to create a revised set of principles before further work was done on the policy. The committee prepared a list of revised principles, which it presented to the ministers of health when they met in September 1989. These principles, drafted without any assistance from or participation by the Red Cross, were accepted by the ministers. They were:

- (i) The voluntary system should be maintained and protected.
- (ii) National self-sufficiency in blood and plasma collections should be encouraged.

- (iii) Adequacy and security of supply of all needed blood components and plasma fractions for Canadians should be encouraged.
- (iv) Safety of all blood, components and plasma fractions should be paramount.
- (v) Gratitude of all blood, components and plasma fractions to recipients within the insured health services of Canada should be maintained.
- (vi) A cost-effective and cost-efficient blood system for Canadians should be encouraged.
- (vii) A national blood program should be maintained.

No further efforts were ever made to create a national blood policy.

In the view of the Red Cross, the purpose of a national blood policy was to identify clearly the roles and responsibilities of the various participants in the blood system, namely, the governments, the hospitals, and the Red Cross itself. In the absence of a national blood policy, no participant could assume a leadership role in the blood system, and accountability for decisions remained unclear. The absence of a national blood policy made it more difficult for the Red Cross to introduce improvements in the blood system and to engage in long-term planning.

The working relationship between the Canadian Blood Committee and the Red Cross

The relationship between the Canadian Blood Committee and the Red Cross began with difficulty and deteriorated. At the heart of the difficulty was the conflict between the principle of independence of the Red Cross and the committee's requirement that the Red Cross be accountable to governments.

The committee's scrutiny of the Red Cross's budget was intense. The committee required line-by-line budgets that listed almost every expense that the Red Cross sought to incur, by province and by blood centre. Line-by-line budgets, the usual practice in the health care sector, particularly for hospitals, restricted the flexibility of the Red Cross but gave government a level of control. Because every province paid for Red Cross blood services within its borders, resources could not be transferred between provinces, or between the national office and the seventeen local blood centres, without the committee's approval. All changes in expenditures from earlier years required clear identification and written justification.

The Red Cross paid the manufacturers of fractionated blood products when the products were received. Until 1983, every province reimbursed the Red Cross for the fractionated blood products used within its boundaries only after the Red Cross had distributed them to hospitals and clinics; the Red Cross was not reimbursed for the financing costs resulting from the delay in the reimbursement by the provinces. Then, in 1983, the Canadian Blood

Committee paid the Red Cross \$500,000 to reimburse it for the financing costs that had accrued during the three previous years. It also developed a new way of paying the Red Cross for fractionated blood products: the provinces paid the Red Cross more than the total cost paid by the Red Cross to the manufacturers, and the money generated by the difference was accumulated in the Red Cross's "fractionation account." Although held in trust by the Red Cross, these funds belonged to the provinces and were kept separate from other Red Cross moneys. The Red Cross paid for the manufacturing, transportation, and financing charges for fractionated blood products from that account, which was replenished as the provinces were billed and then made payment for the products distributed to their hospitals. The Red Cross thus no longer had to use its own assets to pay for any aspect of the fractionation program.

Budget preparation and approval was a long and detailed process. Between 1983 and 1986 the Red Cross formally submitted its budget in September, before the beginning of its financial year on 1 January. In 1986 its financial year was changed to 1 April, to coincide with the government practice. The budget consisted of the consolidated budgets for the local blood donor recruitment programs, the budget for fractionated blood products, and two budgets for the blood transfusion service – one for continuing operating expenses and the other for new programs or expenditures. The budget took the Red Cross five to six months to prepare.

Until 1983, the budget was analysed by the Federal-Provincial Budget and Program Review Committee, which had performed this task before the creation of the Canadian Blood Committee. After 1983, the committee's secretariat assumed this role. The process normally took three to four months. The Red Cross did not directly present its budget to the Canadian Blood Committee. It was always presented by the secretariat, which often recommended reductions in the proposed expenditures. The committee sometimes made additional reductions.

Some members of the Canadian Blood Committee or its subcommittees occasionally suspected that expenditures by the Red Cross were not in accordance with the budget. Two cases are illustrative. In the first instance, in October 1983, one of the members of the Canadian Blood Committee's program and finance committee, which then reviewed the Red Cross's budgets, wrote to the executive director about a proposal for the expansion of the Red Cross management information system:

I am suspicious that the resources currently devoted to systems development and operation (both hardware and manpower) are being diverted to applications and functions other than for the blood program, even though a good portion of the financing for the existing system [was] financed through the blood program allocations.

In the second instance, in June 1985, the Red Cross submitted to the Canadian Blood Committee its implementation plan for testing blood donations for the presence of HIV antibody. The minutes reflect the discussion that then followed:

[T]he CBC [Canadian Blood Committee] [should] limit its approval to what is required to deal with AIDS at this point in time, regardless of the broader programme on blood safety which can be considered within the context of the 1986 budget review process. [A member of the committee] also suggested that the Secretariat look at the proposed budget and monitor actual expenditures to ensure the money is really being spent on the AIDS issue.

The Canadian Blood Committee did not do anything to attempt to investigate these suspicions until the autumn of 1986, when it hired an accounting firm, Touche Ross, to conduct a detailed analysis of Red Cross accounting practices for the years 1982 through 1985. The auditors concluded that the Red Cross accounting system was reliable.

Increasing tensions between the Red Cross and the Canadian Blood Committee

Two new issues emerged in 1983 that imposed additional strains on the relationship between the Red Cross and the Canadian Blood Committee. These issues, the relocation of the Red Cross's head office from Toronto to Ottawa and the purchase of a new computer system, involved significant additional financial commitments beyond those authorized by the budget. The cost of relocation was first estimated to be \$17 million, but later was revised to \$27 million. The computer system was expected to cost \$900,000. In both instances, the Red Cross committed the committee and its member governments to substantial costs without receiving prior approval.

By the early 1980s, the Red Cross had outgrown its national headquarters in Toronto and particularly its national reference laboratory. The laboratory performed several important functions; these included the confirmation of some tests conducted at local centres and the evaluation of test kits. In October 1982, the board of directors decided to move the national headquarters, including the laboratory, to Ottawa. The Canadian Blood Committee was informed of this decision and discussed it when it met in June 1983. Dr Perrault attended the meeting and said that the Red Cross believed it could pay \$8 million of the cost of the move; the money would come from the proceeds of the sale of its existing headquarters and from fundraising. Dr Perrault did not explain to the committee where the Red Cross believed the remainder of the money would come from, although he said it would approach the federal government to pay for part of the laboratory. He said that the Red Cross had already paid a deposit of 10 per cent on part of the land that would be required in Ottawa. At this time, the Red Cross did not

ask the provinces to pay any of the costs of the relocation. The committee told the Red Cross that if it was to be asked to pay any part of the cost, it wanted to be consulted before action was taken. By October 1983, as plans for the move progressed, it appeared that the provinces might indeed be asked to pay for a significant proportion of the cost. The members of the committee expressed their concern at a meeting on 25 October 1983 about "being confronted with a fait accompli with no real choice in the decision."

At approximately the same time, in mid-1983, the Red Cross decided that it needed to improve its computer system. It received what it believed to be a favourable proposal from a manufacturer, but the price quoted was valid for only ninety days. The Red Cross was concerned that, in the time required to prepare a budget submission and receive approval for the expenditure, the price would increase. It therefore entered into a contract to buy the computer and put the cost in its new budget, thus seeking the committee's approval after the fact.

On 22 March 1984, the executive committee of the Canadian Blood Committee met with some Red Cross officials, including Dr Perrault and the secretary general, Mr George Weber, and repeated its desire to be consulted before any decisions involving significant expenditures were made. Dr Perrault said that he had been responsible for informing the committee in June 1983 of the decision to buy the computer, but had forgotten to do so. The minutes of the meeting record that members of the executive committee "stated very clearly that in the future, any decision having an economic impact on the provinces and territories must be taken after consultation with the Canadian Blood Committee." What was meant was that any decision by the Red Cross that would have a significant financial impact on the provinces required the committee's prior approval.

Additional meetings were held between senior officials of the Red Cross and the committee to discuss these issues in particular and, more generally, the effect of the Red Cross's style of decision making on the relationship between the two organizations. The meetings became increasingly tense. On 1 May 1984, six Red Cross officials, including Mr David Balfour, the president, Mr Weber, and Dr Perrault, met with members of the Canadian Blood Committee's executive committee. Mr Balfour said that the need for relocation had been developing for more than fifteen years and that the estimated cost had risen to between \$27 and \$28 million. The Red Cross would raise \$7 million, with the understanding that governments would pay \$20 million. Before the meeting, the Red Cross had issued a press release in which it mentioned the contribution to the project that it expected from governments. The response of the executive committee, as recorded in its minutes of the meeting, was that

no money had been committed for 1984–5 and that funding for 1985–6 will not be considered before a specific proposal is presented to the CBC. It was also made very clear that promotional material committing governments without these governments being aware of it would be a great mistake.

The next day Dr Perrault attended a full meeting of the Canadian Blood Committee. Strong disapproval was expressed about "the fundraising campaign and the promotional material committing governments without these governments being aware of it and having the opportunity to consider a specific proposal." In his report of the meeting to Mr Weber, Dr Perrault commented that

The hostile tone of the meeting was in sharp contrast to the previous evening's session with the Executive. The CBC was undoubtedly briefed by the Executive, but have a responsibility towards their Ministers not to give *any* encouragement to capital projects such as ours. In fact, this is not a surprising situation and they truly fulfilled their duties towards their Ministers.

He went on to recommend that

in the future, no Red Cross representatives should appear *alone* at CBC meetings. A minimum of 2 senior staff members, or of one senior volunteer should be present to assist in moderating what turned out to be real "bear-pit" sessions.

He also recommended that

the CRCS [Canadian Red Cross Society] document for presentation to Governments be professionally prepared by consultants experienced in such issues and that they be tasked by your office in the near future. I am prepared to assist in making preliminary enquiries as to suitable groups. The document would be based on the draft material prepared in-house.
[Emphasis in original.]

In August 1984, the Red Cross presented a brief to the Canadian Blood Committee asking for \$20 million from the provincial and federal governments for its new national headquarters, on the basis that 85 per cent of the space and 80 per cent of the costs were related to the blood program. The committee continued to emphasize that the Red Cross not make decisions about significant allocations of resources without involving the committee.

The tension continued throughout the October 1984–July 1985 period, when decisions were being made about the conversion from non-heat-treated factor concentrates to heat-treated factor concentrates and the funding of HIV-antibody tests. On 29 January 1985, senior officials of the Red Cross met again with the executive committee. The minutes of that meeting illustrate the depth of disagreement that had developed over the involvement of the Canadian Blood Committee in Red Cross decision making. They record

that Mr Hearn, the chairman of the committee, noted that the governments' budget for the Red Cross blood program, which was vital to the Canadian health system, was more than \$100 million. That sum accounted for 100 per cent of the blood transfusion service's costs and 80 per cent of the costs of the blood donor recruitment program. He said that, for the Canadian Blood Committee to fulfil its mandate to governments, it should have a way of participating in a meaningful way in Red Cross decision making. The minutes continue:

Mr Balfour answered that the CBC [Canadian Blood Committee] is receiving adequate information and is in fact monitoring the CRCS [Canadian Red Cross Society] for the Blood Programme; he questioned the reason for such a request. Mr Hearn stated that in a few instances, decisions have been made without participation of the CBC which have created conflicts and which could have been avoided if prior to the Board's decision, the CBC would have been consulted: the VAX computer and the CRCS relocation are two examples. Mr Hearn stated that this issue is twofold: 1) the principle, and 2) the form. If the CBC is allowed to participate in the decision-making, the principle will be satisfied and the form can be addressed.

Mr Balfour retorted that all over the world, Red Cross Societies are operating on the basis of seven principles, one of these being "independence," i.e. absence of control in the decision-making process, especially from governments. He added that the Red Cross is consulting the CBC through the budget approval and that a change in the process would require [it] to alter the fundamental decision-making process at the CRCS, and that the Board of Directors would be opposed to such an orientation.

Mr Hearn finally stated that 1) this [the Committee's involvement in decision-making] is not a simple thought, but a fundamental principle which is there to stay; 2) the CBC is not asking for a vote at the Board of Directors' meeting but is only asking that all issues related directly or indirectly to the Blood Programme be discussed with the CBC before a decision is finalized by the Board of Directors; 3) the form of a mechanism will not be discussed before the principle is accepted.

Mr Dreezer [the CBC representative from Ontario] emphasized that the key issue is the need to find a mechanism of dialoguing with the Red Cross before a decision is made by the Board ...

Mr Balfour said that the position of the CRCS on the relationship CRCS-CBC was given in a December 1982 letter and has not changed. He received instructions from his Board to inform the CBC that this request is unacceptable.

Both parties finally agreed to discuss the issue at a later date.

The relationship between the Red Cross and the Canadian Blood Committee by now was characterized by distrust and poor communication. Approximately one month after this meeting, kits that made it possible to test blood for the presence of HIV antibody became licensed and available in the United States, and the Red Cross began planning the implementation of HIV-antibody testing in Canada. That process required it to cooperate with the Canadian Blood Committee. The committee was also involved in subsequent developments affecting the safety of the blood supply, including the conversion to wet heat-treated factor concentrates and the issue of tests for non-A, non-B hepatitis.

The Canadian Blood Committee was replaced in April 1991 by the Canadian Blood Agency, which continues to exist. Its members are the ministers of health of the provinces and territories, and its objectives are to "direct, coordinate and finance the various elements of the Canadian Blood System requiring national direction" in accordance with the seven principles accepted by the ministers in 1989. It has a finance committee that scrutinizes the finances of the agency and the Red Cross, an executive committee to address management issues, a scientific committee of physicians to give independent expert advice, and, since 1994, a working group on safety in the blood system. Like its predecessor, the Canadian Blood Agency funds the Red Cross blood program, including salaries, equipment in the seventeen blood centres, land and buildings, and most of the costs of donor recruitment; the costs of fractionated products are not included and continue to be apportioned to the provinces according to the amount each province uses.

6

The Bureau of Biologics and the Regulation of Blood and Blood Products

The manufacture, importation, and distribution of blood products are regulated by the federal government, which since 1989 has also regulated the collection, storage, and distribution of blood. These regulatory functions – including the approval of blood products for distribution in Canada, the licensing of manufacturers, and the inspection of collection and manufacturing facilities – are performed principally by a federal bureau known, until May 1996, as the Bureau of Biologics, and now called the Bureau of Biologics and Radiopharmaceuticals. This chapter describes the regulatory functions of the federal government during the 1980s. Because the history is complex and technical, the chapter describes significant developments throughout the decade.

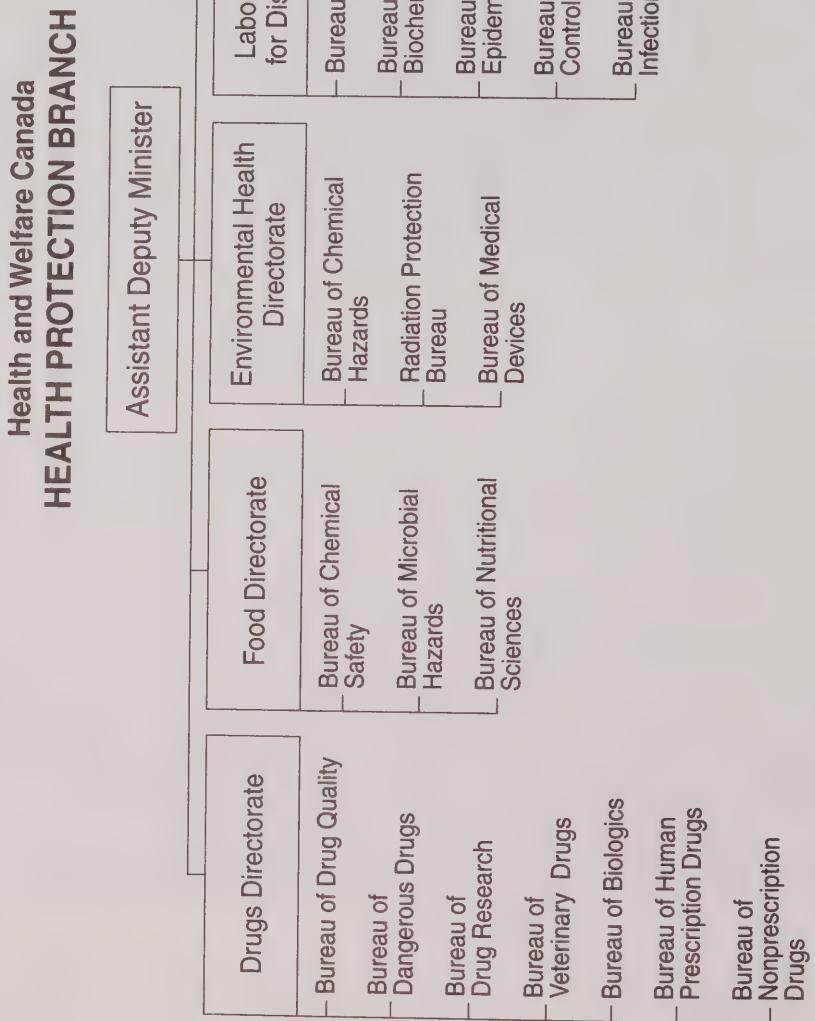
The organization of the federal regulatory authorities

The Health Protection Branch

Throughout the 1980s, the Bureau of Biologics was part of the Health Protection Branch of the Department of National Health and Welfare. The Health Protection Branch exercised regulatory authority over foods, drugs, and environmental matters. It was one of several departmental branches, each of which reported to its own assistant deputy minister. The department has undergone several reorganizations. Several of its programs were moved to other departments in 1993, and in July 1996 all of its welfare programs were formally transferred to the Department of Human Resources. The department containing the remaining health service programs, including those administered by the Health Protection Branch, was renamed the Department of Health.

The Health Protection Branch is divided into several directorates. The organization of the Branch in 1982 is set out in Figure 6.1. Each directorate, with one exception, is charged with the regulatory administration of several health-related federal statutes. One of these statutes is the *Food and Drugs Act*.

Figure 6.1



In 1982, the branch described its approach to the enforcement of the *Food and Drugs Act* as one of “voluntary compliance.” Dr A.B. Morrison, who was then the assistant deputy minister in charge of the Health Protection Branch, had written in 1975 about the culture of voluntary compliance as follows:

We believe our enforcement philosophy must be flexible and respond in an adequate way to enable us to deal individually with unique and complex situations. An overly rigid bureaucracy is no answer to the immensely difficult issues we have to face each day. We prefer to work co-operatively with responsible manufacturers and to encourage voluntary compliance by industry. We try to avoid unnecessary confrontation and adversary proceedings insofar as possible. “Come, let us reason together,” Isaiah said. That sums up what we try to do.

Dr Albert Liston, who succeeded Dr Morrison as assistant deputy minister, testified that the branch promoted voluntary compliance throughout the 1980s. He said that the flexibility it allowed was preferable to issuing regulations and learning that they were not necessary or had become outdated and then having to remove them. He added:

Voluntary compliance is a much more appropriate and efficient and effective way of doing it [regulating]. And by and large, I have to say that voluntary compliance permitted us to extend the purview, to extend the examination of a wider range of areas than would otherwise be possible because regulation and regulatory action is very expensive ...

[W]hen I say “voluntary compliance” you have to take it in the context of when the inspectors come forward with the authority to say, “Do this voluntary compliance, or [else] ...” So basically voluntary compliance has a very strong element of arm twist in it.

The Laboratory Centre for Disease Control

The only non-regulatory directorate of the Health Protection Branch was the Laboratory Centre for Disease Control. It gathered, analysed, and disseminated information about the health of Canadians, and therefore was the central organization for monitoring the appearance and spread of diseases in Canada, principally through its Bureau of Epidemiology. The Bureau of Epidemiology published the *Canada Diseases Weekly Report*, a summary of “current information on infectious and other diseases for surveillance purposes” that was then widely distributed to public health authorities and available to others free, upon request.

Dr Liston called the Laboratory Centre for Disease Control “the eyes of the Health Protection Branch.” In his testimony, he described its role as follows:

Its function was to gather information from a wide variety of sources. It was to provide an appreciation of the health status of Canadians across the country from data that it might obtain from provincial health laboratories, from provincial epidemiologists, from Statistics Canada, from a multiplicity of sources, and act as the centre where this information would be digested, brought together, and perhaps fed back to the provinces ... to provide provincial governments with a comparison relative to the rest of the country ... [This] was intelligence information in the disease surveillance area. We used it, of course, within our own [federal] programs as well ... and relied on it for data on a wide variety of illnesses, communicable diseases.

The Laboratory Centre for Disease Control had an additional responsibility which was very important, and that is the development of analytical methods or laboratory methods which were comparable between one provincial health lab and the next, so that as data was aggregated there would be no distortions because of use of different methods, or methods that were unreliable. So there was a lot of testing ... to make sure that there was a uniformity of laboratory methodology. With the advent of AIDS, the reporting of AIDS cases, et cetera, it was quite appropriate and quite natural for the Laboratory Centre for Disease Control to be involved in that function.

Dr Alastair Clayton was the director general of the Laboratory Centre for Disease Control from January 1979 to July 1987. The offices of the laboratory centre and the Bureau of Biologics were in the same building, and their staff members were in regular communication. As a result, the laboratory centre was a convenient source of information for the bureau about the spread of AIDS and its implications for the safety of the Canadian blood supply.

The Field Operations Directorate

The Field Operations Directorate of the Health Protection Branch enforced compliance with legislative requirements. It conducted most of the branch's routine inspections (one notable exception being inspections of the facilities used by the manufacturers of biological drugs, which were performed by the Bureau of Biologics), investigated irregularities or potential violations of federal legislation in matters within the branch's authority, and assisted in the recall of potentially hazardous products.

The Drugs Directorate

The Drugs Directorate (now called the Therapeutic Products Directorate) of the Health Protection Branch was described at its inception in 1974 as follows:

The Drugs Directorate is responsible for the application of the provisions to the *Food and Drugs Act* and *Regulations* that concern drugs and cosmetics, the *Narcotics Control Act* and *Regulations* and *Proprietary or Patent Medicines Act*. All programs concerned with the manufacturing, marketing, distribution, advertising and surveillance of drugs for use in man and animals are the responsibility of the Drugs Directorate.

Twenty years later, its executive director testified that "essentially, the Drugs Directorate is responsible for the identification, assessment, and management of risks and benefits for all drugs in Canada." These functions included regulating drugs, setting standards for the safety and efficacy of therapeutic drugs, and monitoring compliance with those standards. Within the Drugs Directorate, four bureaus performed these functions, respectively, for prescription drugs, non-prescription drugs, biological drugs, and veterinary drugs. Other bureaus in the directorate dealt with the control of narcotics and psychotropic drugs, quality control, and research.

The Bureau of Biologics

The therapeutic drug industry classifies its products in two broad categories: pharmaceuticals, manufactured from chemical sources; and biologicals, a large and growing collection of therapeutic and prophylactic substances, including vaccines, insulin, and antibiotics, that are produced from biological material, whether human or animal, or from microorganisms. The Bureau of Biologics regulated the biological drugs that were listed in the schedules to the *Food and Drugs Act*.

The Bureau of Biologics was created in 1974, when several divisions in the Laboratory Centre for Disease Control were amalgamated and transferred to the Drugs Directorate, divesting the laboratory centre of any regulatory functions. The bureau's first director, who continued in that office until 1992, was Dr John Furesz, a medical virologist who had been with the Health Protection Branch since 1956. The assistant director from 1976 to 1988 was David Pope, a doctor of veterinary medicine who had previously served in the Bureau of Veterinary Drugs. Dr Pope's functions at the Bureau of Biologics were related chiefly to administration and regulatory affairs.

In 1982, all drugs that were regulated by the Bureau of Biologics, which had previously been listed in three schedules to the Act, were brought together in Schedule D. In that year, "blood derivatives" and "drugs obtained by recombinant DNA procedures" were added to Schedule D. The Bureau of Biologics

did not administer the regulation of biological drugs that were not listed in Schedule D, nor was any other bureau in the Drugs Directorate specifically given this function.

The regulatory functions of the bureau were divided among the Bacterial Products Division, the Viral Products Division, and the Blood Products Division.

The Blood Products Division

The Blood Products Division was created in the late 1970s; before then, blood products were regulated by the Bacterial Products Division, which continued to perform laboratory analysis for the new division until it became fully operational in 1981. Dr Wark Boucher, a virologist who had been with the Bureau of Biologics since 1974, was appointed acting chief of the Blood Products Division in 1982, and chief the next year. When Dr Furesz retired from government service in 1992, Dr Boucher became the acting director of the bureau.

The functions of the Blood Products Division in 1982 were to review submissions from manufacturers seeking licences for drugs derived from blood, to inspect the plants where blood products were manufactured, and to inspect centres in Canada where plasma was collected by plasmapheresis. The federal government did not treat blood and blood components as regulated drugs until "blood" was expressly added to Schedule D in September 1989. Until then, standards of health and safety and of quality assurance in the collection, testing, processing, storage, and distribution of whole blood and its components were in the hands of the operator of the blood system, the Canadian Red Cross Society (Red Cross).

The U.S. regulator

Since 1972, the regulation of blood and blood products in the United States has been conducted by the Food and Drug Administration, a division of the Public Health Service within the federal Department of Health and Human Services. Like those of the Health Protection Branch, the activities of the Food and Drug Administration are directed to protecting the health of the nation against impure and unsafe foods, drugs and cosmetics, and other related hazards. In the Food and Drug Administration, the regulation of the collection, processing, testing, and marketing of blood and blood products was performed by the U.S. Bureau of Biologics until an administrative reorganization of the Food and Drug Administration in 1982. The Center for Drugs and Biologics was created at that time, and the regulation of blood, blood products, and blood-banking technologies fell under the purview of the Office of Biologics Research and Review in the center. In 1988, following another reorganization, the Center for Biologics and Review assumed the functions previously performed by the Office of Biologics Research and Review. In 1993, the Center for Biologics and Review was renamed the Center for Biologics Evaluation and Research.

The Food and Drug Administration makes extensive use of technical advisory committees to assist it in the evaluation and regulation of drugs, biologics, and medical devices. One of these, the blood products advisory committee, evaluates data and makes appropriate recommendations related to the safety, effectiveness, and labelling of blood and blood products. During the 1980s, the blood products advisory committee was composed of experts drawn from the blood-banking and fractionation industries and a wide range of other disciplines, including public health, transfusion medicine, biochemistry, infectious diseases, virology, hematology, and oncology. The blood products advisory committee serves as a standing committee to the Center for Biologics Evaluation and Research.

The legislative framework

The regulation of blood and blood products in Canada is governed by the provisions of the *Food and Drugs Act*, a federal statute. Under the *Constitution Act, 1867*, Parliament has the power, though not an express power, to enact legislation to prevent harm to the health of Canadians, and the *Act* is an exercise of this power.

The Food and Drugs Act

The origin of the *Food and Drugs Act* is in federal statutes that dealt with the hazards associated with the sale of adulterated food and beverages and deceptive practices in the sale of those products. The first of these statutes was the *Inland Revenue Act of 1875*. Amendments extended the authority of that *Act* to drugs. In 1884, the protections afforded by this *Act*, along with other protections, were recast as the *Adulteration Act*. It in turn was replaced in 1920 by the first *Food and Drugs Act*, which has since been amended frequently. One amendment, in 1927, required the manufacturers of scheduled biological preparations to be licensed. Another, enacted in 1951 and extensively revised in 1962, required manufacturers to file a submission supporting the safety of a “new drug” and to obtain government approval before the drug could be marketed.

The *Food and Drugs Act* defines “drug” broadly as including

any substance or mixture of substances manufactured, sold or represented for use in

- (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state, or the symptoms thereof, in man or animal,
- (b) restoring, correcting or modifying organic functions in man or animal, or
- (c) disinfection in premises in which food is manufactured, prepared or kept.

The term “sell” is defined as including “offer for sale, expose for sale, have in possession for sale and distribute, whether or not the distribution is made for consideration.” All blood-related products – whole blood, components, plasma, plasma derivatives, coagulation factor concentrates, and all other fractionated substances – come within the broad definition of “drug.” Any distribution of blood, blood components, or products made from or with blood comes within the statutory meaning of “sell,” even if the distribution is made without charge.

Section 8 of the *Act* prohibits the sale of any drug that was manufactured, prepared, preserved, packaged, or stored under unsanitary conditions or is adulterated. Section 9 prohibits the labelling, packaging, treating, processing, selling, or advertising of any drug in a manner that is false, misleading, or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit, or safety. Section 12 prohibits the sale of certain classes of drugs, unless their manufacturing premises and the processes and conditions of manufacture have been approved in order to ensure that these drugs are not unsafe. It reads as follows:

No person shall sell any drug described in Schedule C or D unless the Minister has, in prescribed form and manner, indicated that the premises in which the drug was manufactured and the process and conditions of manufacture therein are suitable to ensure that the drug will not be unsafe for use.

These sections of the *Act*, as described, were in force in 1982.

The word “Minister,” as it appears throughout the *Act* and its *Regulations*, in the 1980s referred to the Minister of National Health and Welfare. In most matters of administration, a Minister of the Crown acts through public servants employed in his or her department, including, in the case of the Department of Health and Welfare, the employees of the Bureau of Biologics. The “powers, duties and functions” assigned to the Minister by the *Department of National Health and Welfare Act* included “all matters relating to the promotion or preservation of the health ... of the people of Canada over which the Parliament of Canada has jurisdiction.” These “powers, duties and functions” were executed and performed by the members of the department’s staff.

The *Food and Drugs Act* had no application to drugs that were neither manufactured nor sold for consumption in Canada. There was an active trade in the trans-shipment of blood-related products by some Canadian firms in the 1970s and 1980s. Montreal was one of two or three global centres involved in the “international plasma trade.” The Bureau of Biologics did not regulate this trade, nor were the Canadian brokers who redirected foreign blood-related products through Montreal required to notify the bureau about their

dealings or maintain any records of the transactions. During the same period in the United States, the export of biological products was regulated by the U.S. counterpart of the Bureau of Biologics.

The Food and Drug Regulations

The *Food and Drugs Act* has been described as "deceptively simple." The details are set out in several schedules to the *Act* and in complex regulations made under the *Act*. The *Food and Drug Regulations* set out the regulatory functions exercised by the Minister. They are made under the authority of section 30 of the *Act*, which authorizes the Governor in Council to make regulations for carrying the purposes and provisions of the *Act* into effect. Parts of the *Regulations* are broad in application, while others refer only to narrow classes of drugs. While there have been many amendments to specific provisions since then, the general organization of the *Regulations* is the same today as it was in 1982.

The *Food and Drug Regulations* are divided into "parts," most of which are subdivided into "divisions." Several of the parts are devoted to categories of commodities (such as "Foods," "Drugs," and "Vitamins") governed by the *Act*. Part A, "Administration," is of general application. It contains the definitions of several terms that appear in the *Regulations*. A "manufacturer" is defined as any person, including a firm, partnership, or corporation, "who under his own name or under a trade, design or word mark, trade name or other name, word or mark controlled by him sells a food or drug." The Red Cross, as a distributor of blood (a "drug," as defined in the *Act*), came within the general definition of manufacturer in the *Regulations*.

Division 4 of Part C, which governs the biological drugs listed in Schedule D, contained a different definition of "manufacturer"; and the general definition of "manufacturer" did not apply to the matters governed by that division. As noted, "blood" was not included in Schedule D until September 1989. Dr Pope testified that "with respect to all parts of the *Regulations* but for Division 3 [which deals exclusively with radiopharmaceutical drugs] and Division 4 of Part C, whenever the word 'manufacturer' appears it indeed applies to the Canadian Red Cross."

Part C deals with "Drugs" and contains ten divisions. Division 1, "General," applies to all drugs governed by the *Act*. Division 2 is entitled "Good Manufacturing Practices." Its provisions, introduced in 1982, are intended to ensure that the drug products distributed in Canada are of consistent quality. They prohibit any manufacturer or importer from selling a drug unless it has been produced in accordance with certain requirements, set out in that division, that govern the production and packaging of drugs – including the premises in which the drugs are manufactured, the equipment and personnel involved in their manufacture, the testing of raw material and finished products, manufacturing processes and quality control, and storage and record keeping.

Division 2 did not apply to "blood derivatives" or any other category of drugs listed in Schedule D to the *Act* until 1 January 1997. An "information letter" containing draft legislation to extend good manufacturing practices to drugs governed by Division 4 had been distributed to drug manufacturers by the Health Protection Branch thirteen years earlier, in August 1984.

Unlike "blood derivatives," the collection and processing of "blood" for distribution were subject to the Division 2 regulations governing good manufacturing practices. This continued until "blood" was exempted from the application of Division 2 through its addition to Schedule D in 1989.

Because "blood" was not included in Schedule D, the Bureau of Biologics did not assume any authority to administer the *Regulations* in regard to blood before 1989. As Dr Pope testified, "the Bureau [of Biologics] can only act within the limitations of the drugs listed in Schedule D," and "blood" was not then one of the listed drugs. No other bureau in the Drugs Directorate or elsewhere in the Health Protection Branch administered or enforced the provisions for good manufacturing practices at the facilities of the Red Cross blood transfusion service during the 1980s.

Divisions 4 and 8 of Part C govern the regulation of biological drugs and the manufacturers of these products, and are therefore of fundamental importance to the safety of blood-related substances listed in Schedule D.

Division 8, "New Drugs," applies to all drugs, both pharmaceuticals and the biological drugs listed in Schedule D. It sets out the requirements for applications for departmental authorization to distribute new drugs in Canada for sale, clinical trial, or emergency treatment. The manufacturer of a drug that has been authorized for commercial distribution is issued a "notice of compliance," without which it is not entitled to sell the drug.

In the ordinary course, the manufacturer of a drug for which a notice of compliance had been issued could then begin to sell or otherwise distribute the drug. However, there were additional requirements – as prescribed by Division 4 of Part C of the *Regulations* – for drugs listed in Schedule D. No manufacturer could distribute a Schedule D drug unless, in addition to a notice of compliance, the manufacturer had been issued a licence under Division 4 and samples from the lots intended to be sold in Canada had been tested and authorized for release. The licence authorized the manufacturer to sell in Canada the Schedule D drugs that were listed in the licence. The lot release authorized the manufacturer to distribute in Canada vials of the licensed drug that were manufactured from the same lot from which the sample vials were tested. These additional precautions of licensing and lot-by-lot testing and release were taken because the drugs listed in Schedule D, being of biological origin, are much more variable and pose a greater risk to the health of consumers than do pharmaceutical drugs of purely chemical origin. The Schedule D drugs are regulated more closely for quality, potency, and safety than are pharmaceutical drugs.

The provisions of Divisions 8 and 4, as they were in 1982, are discussed in the following sections.

Division 8 of Part C of the Food and Drug Regulations: "New Drugs"

Division 8 described the procedures through which the Health Protection Branch authorized the sale of "new drugs" – that is, new chemical entities, new mixtures of existing drugs, and existing drugs for which a new use or condition of use was proposed. Except for authorized emergency treatment, a new drug could not be distributed until the manufacturer filed a "new drug submission" with the Minister and received a notice (the "notice of compliance") that the submission complied with the regulatory requirements. A "new drug" was defined in the *Regulations* as meaning:

- (a) a drug that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug;
- (b) a drug that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in that combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or
- (c) a drug, with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration, or duration of action and that has not been sold for that use or condition of use in Canada, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug.

A new drug submission required extensive documentation, often amounting to many thousands of pages. The information that was required included a description of the new drug; the name under which it was to be sold; the quantitative formulation of the drug; the specifications of the ingredients (and, where requested, the names and addresses of the manufacturers of those ingredients); a description of the plant and equipment to be used in manufacturing the drug; a detailed description of the method of manufacture; details of the tests to be applied to control the potency, purity, stability, and safety of the drug; detailed reports of the tests made to establish the clinical safety of the drug; evidence of the clinical effectiveness of the drug; the names and qualifications of the clinical investigators; drafts of the product labels; a statement of the proposed promotional presentations; a description of the pharmaceutical form in which the drug was to be sold; and samples

of the finished product. If, after a notice of compliance was issued, there was a significant change from the original information given to the branch, the drug could not continue to be sold unless the manufacturer submitted an appropriate "supplementary new drug submission" and received in turn a new or amended notice of compliance.

The review of every new drug submission was conducted by the bureau in the Drugs Directorate that regulated drugs of the same class. For example, submissions of new drugs intended for veterinary use were reviewed by the Bureau of Veterinary Drugs. Those that involved drugs listed in Schedule D to the *Act*, including scheduled blood-related products, were reviewed by the Bureau of Biologics. The bureau involved reviewed the documentation submitted by the manufacturer, with particular attention given to the integrity of the manufacturing process and the supporting clinical data. The bureau that conducted the review issued the notice of compliance only when it was satisfied that the manufacturer's submission or its supplement complied with the regulatory requirements.

During his testimony, Dr Liston explained that a notice of compliance is not a drug approval:

It is a notice that a manufacturer has supplied sufficient information to the regulatory body to demonstrate that the drug can be used with a certain patient population, with a risk-benefit ratio that has been deemed to be beneficial. That means that under the conditions that the manufacturer ... puts forward [in its submission] ... that the conditions of manufacture, the staff involved with it, the quality of the plant, the air turnover, all of these things have been found to be adequate ...

So the notice of compliance says under these conditions we believe that this legal entity [the manufacturer or its agent] has a product which is or which can be used safely under certain conditions.

Except for radiopharmaceuticals and the biological drugs listed in Schedule D (for which there were additional requirements, discussed below), after a notice of compliance was issued for a drug its manufacturer could begin to sell or otherwise distribute it in Canada. A manufacturer was required to maintain records of investigations, studies, and published scientific reports concerning each new drug for which it had been issued a notice of compliance. Records of drug mixture or adulteration, a labelling error, or a significant chemical or physical change or deterioration in a lot of a new drug were to be forwarded to the branch immediately upon their receipt by the manufacturer. Unexpected side-effects, injuries, toxicity, or sensitivity associated with the use of a new drug, or a failure to achieve its expected pharmacological activity, were to be reported within fifteen days.

Manufacturers planning to sell a new drug were required to conduct clinical trials to establish the safety, dosage, and effectiveness of the product.

If a manufacturer wished to conduct a clinical trial in Canada, it had to file what was called an "investigational new drug submission" or "pre-clinical submission" with the Health Protection Branch. The submission included a detailed description of the purposes, procedures, and methodology of the trial. If the trial was authorized, the drug could be used in Canada, but solely for the purpose that had been approved. The regulations regarding pre-clinical submissions applied to all new drugs, including those listed in Schedule D.

A physician who wanted to treat a patient with a drug for which no notice of compliance had been issued could apply to the Health Protection Branch, under the "emergency drug release" program, for a letter authorizing the sale to the physician of a specified quantity of the drug for the emergency treatment of his or her patient or patients. In the case of blood-related products, the application was reviewed and the letter issued by the Bureau of Biologics. The sale of a new drug for emergency treatment was "exempt from the provisions of the Act and the Regulations."

Division 4 of Part C of the Food and Drug Regulations: Schedule D Drugs

Division 4 of Part C of the *Regulations* was concerned principally with the safety of the biological drugs listed in Schedule D to the *Act*, including scheduled blood-related products. It established the means by which the Minister might be satisfied that, as contemplated by section 12 of the *Act*, the premises and process and conditions of manufacture "are suitable to ensure that the drug will not be unsafe for use." When the Minister – in practice, the Bureau of Biologics – was satisfied, a licence to this effect was issued to the manufacturer. The licence had to be renewed annually.

The extra safeguards prescribed in Division 4 were intended to protect consumers of Schedule D drugs from the risks associated with the use of biological drugs. The source material for a biological drug may contain disease-causing organisms (pathogens) that can be transmitted to and may infect a person treated with the drug. Large-scale manufacturing of most biological drugs requires the pooling of source material from hundreds or thousands of persons or animals. If the source material from even one of the donors contains infective pathogens, the entire pool and all the drugs produced from it may be contaminated. To reduce the risk of transmission of a disease through biological drugs, the manufacturer must establish and follow procedures that will preclude or at least minimize the collection of infected source material and reduce the probability or extent of contamination of any pooled biological material. The manufacturer must also take measures during the processing of the material to ensure that no new contamination occurs and, in some instances, to inactivate pathogens that may be in the source material. Because the pharmacological activity of the source material varies, if only slightly, from donor to donor, the manufacturer must also ensure that the individual units it produces are consistent in quality, efficacy, and safety. These matters are dealt with in Division 4.

The ambit of regulatory control afforded by Division 4

The additional consumer protection afforded by Division 4 extended only to the drugs listed in Schedule D and to the manufacturers that were issued a licence for those drugs. Except for radiopharmaceutical drugs, both “drug” and “manufacturer” were defined more narrowly in Division 4 than elsewhere in Part C of the *Regulations*, which governs drugs. A “manufacturer” was defined as one “to whom a licence has been issued as provided in this Division.” A Division 4 licence was issued only for the drugs governed by Division 4, and “drug” was defined to mean only those drugs “mentioned or described in Schedule D.” If a drug was not included in Schedule D – even if it was commonly understood to be a biological drug – it was not subject to the extra safeguards, including the licensing of its manufacturer, prescribed by Division 4. As previously pointed out, before 1989, “blood” was not expressly included in Schedule D or in any other schedule to the *Act* or its *Regulations*.

In 1953, “sera and drugs analogous thereto for parenteral use” were added to Schedule D. In 1969, these words were amended to read “sera and drugs analogous thereto.” Before 1978, only three classes of drugs were listed in Schedule D – drugs, other than antibiotics, prepared from microorganisms; sera and drugs analogous thereto; and antibiotics for parenteral use.

Of these, only the second was in any way related to blood or blood products. The Bureau of Biologics consistently interpreted “sera and drugs analogous thereto” as meaning blood products that were fractionated from plasma, including albumin, immune globulins, and the coagulant blood products, such as factor VIII and factor IX concentrates, that were used by hemophiliacs. The term was not interpreted as including whole blood or blood components, including plasma. As the fractionation industry evolved and new therapeutic applications of plasma-derived products were developed, the phrase “sera and drugs analogous thereto” increasingly came to be viewed as imprecise. In 1982, Schedule D was extensively amended and, in one of the changes, “sera and drugs analogous thereto” was replaced by “blood derivatives.”

Dr Pope, the assistant director of the Bureau of Biologics at the time of the amendment, testified that “in the minds of the Bureau” there was no “difference between ‘blood derivatives’ and the phrase it replaced.” Neither phrase was considered by the bureau as including whole blood or blood components, including plasma. Dr Pope agreed that, on a “dictionary” interpretation, “anything that is derived from blood is a ‘blood derivative.’” However, he said,

it is not the way the word was being used and this is the essential point in the drug industry and also in the regulatory agencies around the world at this time. They were always using this word “blood derivatives” and were not applying it to everything that was a derivative.

According to both Dr Pope and Dr Furesz, the approach taken by the Bureau of Biologics in 1982 to the scope of its regulatory authority with respect to blood-related material was that

blood derivatives were what the fractionators produced and were therefore regulated by the Bureau, and blood components were what the Red Cross blood transfusion service produced and were therefore unregulated by the Bureau of Biologics.

For the Bureau of Biologics, then, "blood derivatives" were the fractionated products made from plasma and not the plasma itself. The one exception was "human plasma collected by plasmapheresis" (often referred to as "source plasma"), which was added to Schedule D on 15 November 1978. Plasmapheresis was a relatively new method of collecting plasma (the yellowish, liquid portion of blood) in which the other components, including the red cells, were returned to the donor during the procedure. Although the Red Cross permitted donors of whole blood to donate blood only once every three months, it was not uncommon for donors undergoing plasmapheresis to be "bled" weekly or semi-weekly. In the United States there were many commercial plasmapheresis centres, where donors were paid for their plasma. Several similar centres opened in Canada in the early 1970s. None of them was then subject to regulation by the Bureau of Biologics.

Until the arrival of the commercial plasmapheresis centres, the Red Cross had a de facto monopoly on the collection of blood and plasma in Canada. The Red Cross was a well-respected charitable organization that was believed to have the ability to regulate itself. In contrast, the plasmapheresis centres were seen as purely commercial enterprises with neither history nor experience to attract public confidence. In November 1973, the assistant deputy minister in charge of the Health Protection Branch established an expert committee "to examine Canadian Regulations concerning plasmapheresis." The committee concluded that, when practised unscrupulously, plasmapheresis posed "real dangers to the health of the donor," and that there were also "hazards to users of the plasma or its derivatives ... from, among other things, hepatitis." In a report dated 21 April 1975, the committee recommended that plasmapheresis centres be regulated and the centres licensed. These recommendations led to the decision to add "human plasma collected by plasmapheresis" to Schedule D and associated regulations to Division 4 in 1978. There were then fewer than six commercial plasmapheresis centres in the country and, as Dr Furesz, the director of the Bureau of Biologics at the time, testified, their collections constituted "an extremely tiny proportion of all the plasma that was being collected in Canada." However, the new regulations were of universal application. They extended to all plasmapheresis centres, including those that would soon be operated by the Red Cross, collecting plasma from volunteer donors.

In the United States, by the late 1970s, most of the plasma used to manufacture fractionated blood products was collected by plasmapheresis. In Canada, the Red Cross did not begin to collect source plasma for fractionation until the early 1980s, and until 1986 more than 90 per cent of the plasma sent for fractionation by the Red Cross was "recovered plasma" that had been separated from donations of whole blood. Recovered plasma – like whole blood and blood components – was not on any schedule and, until September 1989, remained outside the regulatory control of the Bureau of Biologics. At that time, Schedule D was amended to replace "blood derivatives" with "blood and blood derivatives."

Because it distributed "drugs," as defined in the *Food and Drugs Act*, the Red Cross was a "manufacturer" in the broad sense defined in Part A of the *Regulations*, and was thus subject to the regulations of general application that applied to every distributor of drugs. However, until source plasma was added to Schedule D in 1978, the Red Cross was not a "manufacturer" within the narrower meaning of Division 4 of Part C and was not subject to the licensing requirements and the regulatory control of the Bureau of Biologics, which administered that division. Even then, the bureau's regulatory control over the Red Cross extended only to its plasmapheresis centres – a very small portion of its blood-related operations. There was no regulatory control over most of the operations of the Red Cross blood transfusion service until "blood" was added to Schedule D in 1989.

Division 4: The general provisions

Division 4 of Part C of the *Regulations* contained general provisions that applied to the manufacture of all drugs listed in Schedule D, and provisions that applied only to limited types or classes of scheduled biological drugs. Two sets of these limited provisions were of particular relevance to the production of blood products. One was entitled "Preparations from Human Sources"; the other, "Human Plasma Collected by Plasmapheresis." These two sets of provisions are described separately below.

The applicant for a licence issued under Division 4 was required to submit information to the bureau about "the drug in respect of which an application for [the] licence is made," including a description of the manufacturing premises and manufacturing process, the names and addresses of the Canadian distributors and agents, and the names and qualifications of the manufacturer's employees who were responsible for the manufacture and testing of the drug. In addition, as "a condition of the issuance and continuation of a licence," the bureau could require a manufacturer to submit to a physical inspection of its premises and manufacturing process, the qualifications of the firm's technical staff, and the firm's "records relevant to the drug," and could require samples of materials used in the process of production and of the finished product. A licence that was issued to a manufacturer listed all that manufacturer's drugs to which the licence related. The licence could be cancelled

or suspended, either entirely or in respect of any of the drugs for which it was issued. The bureau could impose such conditions for the reinstatement of the licence or the removal of the suspension as it considered "necessary to ensure that any drug for which the licence [was] issued will not be unsafe for use."

A manufacturer was obliged to keep and maintain records of the manufacture, testing, and distribution of every lot of a drug that it was licensed to manufacture, and to make these records available to the bureau "on request." Upon written request, a manufacturer was also required to submit "protocols of tests together with samples of any lot of any drug prior to its being sold." No drugs from the lot could be sold if the protocol or sample failed to meet the regulatory requirements. These "lot" requirements were unique to Schedule D drugs and reflected the concern for variations in potency, safety, and quality that were more likely to occur in drugs manufactured from a biological source than in drugs derived from chemicals. In practice, samples of lots of Schedule D drugs were routinely reviewed by the Bureau of Biologics before their release was authorized. The bureau's practice in the 1980s was described in a paper written by Dr Boucher and Dr Furesz:

Manufacturers are required to obtain authorization from the Bureau for the sale of each lot of each licensed product they sell. In order to obtain such authorization the manufacturer has to submit samples of the finished drug and, if requested, materials used in its production together with reports on the results of his testing of the lot in question. The submitted samples are tested in the Bureau laboratories in order to confirm the manufacturers' findings. These tests include those that are specific for determining the identity, potency and purity of individual products. Pyrogen testing [to determine whether a substance causes fever] is conducted in rabbits and for some products the limulus amoebocyte lysate assay [for a specific pyrogen] is used. General safety [toxicity] of most products is determined in guinea pigs and mice. Only when all testing is satisfactory is authorization for sale granted.

Every manufacturer informed the bureau of its specifications for each of its products. It then submitted, by way of a "certificate of analysis," the results of studies and tests demonstrating that every lot of each of its products intended for distribution in Canada met the specifications. The bureau's lot-by-lot testing did not include testing for viral contamination or viral inactivation. The bureau conducted a comparative review, ensuring that the samples submitted by the manufacturer met some of the specifications set out in the certificate of analysis that accompanied them. A manufacturer was required to notify the bureau promptly of any changes in the "responsible qualified personnel, the premises in which the drug is manufactured, and [the] process and conditions of manufacture." It was also required to notify

the bureau of any deficiency or alleged deficiency in the quality, safety, or efficacy of any drug it manufactured. The bureau relied on the manufacturer for information of this nature. Dr Boucher, the chief of the bureau's blood products division through most of the 1980s, testified that

[p]ost-market surveillance is ... a responsibility of the manufacturer. It is not something that we in the Bureau had the resources to do ... So we would depend on the [manufacturing] company to gather information.

The bureau did not maintain any record of the distribution of a drug after it had authorized the release of the lot from which it was produced. "My responsibility," Dr Boucher testified, was "the release and testing of the lot. How much of the lot was sold on the market, or how much was on the market ... I did not monitor the distribution, how much was left, what was used, what wasn't used."

Packages of licensed drugs were required to bear labels containing specified information for consumers, including the name of the manufacturer, the potency and recommended dose of the drug, the lot number, and adequate directions for the use of the drug. There was no requirement that the labels include information about appropriate and inappropriate uses of the drug, precautions, or side-effects associated with the use of the drug. If the drug was derived from human sources, both the inner and outer labels had to say so clearly. The "inner label" meant the "label on or affixed to an immediate container" of a drug; the "outer label" meant the label "on or affixed to the outside of a package" of a drug.

Division 4: Preparations from human sources

Manufacturers of "preparations from human sources" were subject to additional regulatory requirements set out in Division 4. These "preparations" were not included in Schedule D and were not therefore "drugs" within the meaning of that word in Division 4. However, manufacturers were subject to stringent requirements when these preparations were used in the production of a drug listed in Schedule D. "Preparations from human sources" were defined as "pooled blood plasma, or pooled blood serum, or fractions of either separated by a method satisfactory to the Minister." Manufacturers were permitted to obtain human serum or plasma only from persons who had been certified by a qualified physician as healthy. They could not use blood donors who had a history of a disease transmissible by blood transfusion, including syphilis, infectious hepatitis, and malaria. The drawing of blood from a donor was to be conducted under the supervision of a qualified physician in a "suitable bleeding room" under the manufacturer's control. A manufacturer of preparations from human sources was required to maintain a complete record of all its donors, including their certificates of good health.

As previously noted, with the exception of human plasma collected by plasmapheresis, the Red Cross was not a "manufacturer" as defined by Division 4 until "blood" was added to Schedule D in September 1989. As a result, the Red Cross, in the management of its blood collection and distribution operations, was not directly obliged to comply with the regulations respecting "preparations from human sources" until 1989. However, these regulations applied to the producers of fractionated blood products, including the factor concentrates used by Canadian hemophiliacs, by virtue of these products' inclusion in the classes of drugs listed in Schedule D. These producers were "manufacturers" for the purpose of Division 4, and the products that they manufactured included those made from pooled plasma – a "preparation from human sources" – that had been recovered from blood donations collected by the Red Cross.

With some exceptions, the manufacturers of fractionated blood products did not themselves collect their essential ingredient, human plasma, directly from blood and plasma donors. Most often, they purchased the plasma collected by wholly owned subsidiaries or by the independent operators of plasmapheresis facilities, or they "custom fractionated" the plasma collected by others, such as the Red Cross, in return for a processing fee. Yet, as the licensed manufacturer of Schedule D drugs, it was the fractionator (even though not in Canada), and not the plasma collector, that was required to meet the regulatory obligations for "preparations from human sources." A manufacturer could meet its obligations only by ensuring that the plasma collectors from which it obtained its plasma – including the Red Cross – were themselves in compliance with these regulations. The enforcement of these regulations by the Bureau of Biologics was, Dr Pope testified, "via the manufacturer by requiring that the manufacturer use plasma that met these conditions."

The bureau relied on the manufacturers to observe the regulatory criteria for preparations from human sources. The manufacturer was required to supply the bureau with, or at least maintain, records related to the safety of the plasma that it processed into blood products. The bureau conducted occasional inspections at the fractionators' manufacturing premises, but it did not inspect the facilities where the plasma used by the fractionators was collected. The "question," as framed by Dr Furesz during the course of his testimony, was "how is the Bureau of Biologics discharging its regulatory activity with the fractionator as far as the source material is concerned?" His answer included the following comments:

When we are talking about what I would call the classical fractionators, we considered the Red Cross plasma as a source material. So it was on the onus of the fractionator to make sure that all the sources of that [material] do comply with our Division 4 regulations ...

Biological drug manufacturers, not [only] fractionators, any kind of manufacturer are responsible by our regulations for ... the quality, and you can call it safety as well, of the raw materials which go into their product. We cannot regulate all the individual providers of source materials. That was technically impossible, which I don't have to go into. In other words, we do delegate the responsibility [to] the manufacturer that he will make sure that all the source materials are of the highest quality ...

It is not only a question of trust. It [the manufacturer] has to prove to us [the bureau] with all the documents that they have done the proper – if it is needed – inspection, or quality control testing ...

Our role is to make sure that the manufacturer is presenting us true and not false statements, and procedures, and [that] the submission is really true. As long as the manufacturer can prove this to us, we have to have confidence in the manufacturer ... There is no way that we can spread out and have all [licensed manufacturers of Schedule D drugs] under the closest scrutiny. We have to accept their submissions, and we have to make sure when they get their raw materials – which, in this case, happens to be plasma – [that it] is taken according to our regulations.

The bureau acknowledged that the regulations governing preparations from human sources gave it the authority to require manufacturers to institute measures to screen out donors who were potentially infected with blood-borne diseases. It did not institute this requirement with respect to AIDS at any time through the 1980s. Nor did the bureau's inspections of manufacturers include requests to see records of measures taken to screen donors for AIDS. Dr Furesz said:

[T]o my best knowledge, all fractionators were aware of all those questions about AIDS at that time ...

[U]nder this regulation we felt it was the manufacturer's duty to know what to look for, how things are changing ... [W]e expect the fractionator as a licensed manufacturer to know what to do and what to look for.

Division 4: Human plasma collected by plasmapheresis

The comprehensive regulations governing "human plasma collected by plasmapheresis" were added to Division 4 when "human plasma collected by plasmapheresis" was added to Schedule D late in 1978. The addition made both commercial plasmapheresis centres and those soon to be operated by the Red Cross subject to the regulatory control of the Bureau of Biologics. They were obliged to meet the licensing requirements prescribed in Division 4 and, on receipt of a licence, were "manufacturers" as defined in and regulated by the provisions of that division.

Some of the provisions governing plasmapheresis were designed to protect the health of the donor. Before enrolling in a plasmapheresis program, prospective donors had to be examined carefully by a physician and told of the hazards of participation. Any prospective donor who appeared to be under the influence of alcohol or drugs, or who did not appear to be answering questions reliably, was to be rejected. At first, a physician was required to be present throughout every collection, but this requirement was soon amended to require only that a "fully informed" physician be available "within ten minutes of the time the need arises." The regulations restricted the frequency of donations of plasma from any donor to no more than two within forty-eight hours and four within any seven-day period, and they imposed a maximum volume that could be collected from a donor at one time and within any six-month period. Special precautions were to be taken to prevent any infection of the donor as a result of the procedure, and each donor's records were to be reviewed by a physician at least every three months "to determine the continuing suitability of the donor to remain on the program."

Other provisions were intended to protect the health of potential recipients of the plasma collected by plasmapheresis or, as was more likely to be the case, the recipients of fractionated products manufactured from the plasma. On the day the plasma was to be collected, a physician or trained person acting under the physician's supervision was first to interview and evaluate the donor to ensure, among other things, that the donor was free from infection with any disease that might "create a risk of contamination" of the plasma, any disease transmissible by blood transfusion, and any skin punctures or scars indicative of drug addiction. The examiner was also to ensure, on each occasion, that the prospective donor had no history of viral hepatitis, had not been in close contact with someone suffering from viral hepatitis within the previous six months, and had not within the same six months received blood or any blood derivative that was a possible source of viral hepatitis. Every unit of plasma was to be non-reactive to a test for the hepatitis B antigen. A donor found at any time to be unsuitable was to be immediately removed from the program.

Every licensed operator of a plasmapheresis program was required to maintain complete records of all examinations, evaluations, reviews, and interviews of donors and all laboratory tests conducted, and every donor's record was to be cross-referenced to the units of plasma given by that donor. Every operator was also required to establish a system that "positively identifies each donor and relates the records and laboratory data of each donor directly to the donor's blood and its components." The operator had to use a photograph or some other method of "equal assurance" to confirm every donor's identity. Each container of blood and plasma had to be identified in a manner "so as to relate it directly to the donor."

None of these comprehensive regulations applied to donations of whole blood or the components, including plasma, separated from whole blood. When "blood" was added to Schedule D in September 1989, there were no related additions or amendments to Division 4 of Part C of the *Regulations*. There are still no regulations that relate only to the collection, processing, and distribution of whole blood or the plasma separated from whole blood. These substances remain subject only to the general regulations that apply to all drugs listed in Schedule D and the provisions that govern drugs manufactured from "preparations from human sources." In 1992, the Drugs Directorate published a document entitled "Blood Collection and Blood Component Manufacturing." Its preface reads:

This guideline provides reference standards and defines minimum criteria for facilities in Canada that collect blood and manufacture blood components. The principles and practices described herein are acceptable to the Health Protection Branch (HPB) for the manufacture of blood and blood components. Observance of these guidelines should ensure compliance with the appropriate standards and regulations.

In the United States, the collection, processing, and distribution of blood and blood products have been regulated as drugs since the early 1970s.

In September 1983, a commercial plasmapheresis centre in Nova Scotia told the Bureau of Biologics about the detailed procedures it had established to reduce the risk of collecting plasma contaminated with AIDS. Its procedures included a physical examination of and an interview with every donor, designed to identify and exclude persons who might be infected with AIDS, and educational material that encouraged prospective donors who were at high risk of contracting AIDS to withdraw voluntarily from giving plasma. Dr Boucher, the chief of the Blood Products Division, agreed that these procedures "went some way to identifying and screening out persons who might be at risk of infecting a plasma donor pool." No similar AIDS-related measures were taken at the Red Cross's plasmapheresis facilities, nor did the bureau ever require or request that the Red Cross adopt similar procedures. Dr Boucher testified that the bureau "left this up to the Canadian Red Cross." In his testimony, Dr Furesz said that "[w]ith the plasmapheresis part of it, where we had the regulatory mandate to do it, I would say, yes, we did not specify explicitly as maybe we should have done."

Removing potentially hazardous drugs from the marketplace

The removal of potentially hazardous products from the marketplace – including those that were otherwise governed by the *Food and Drugs Act* – was normally initiated by the manufacturer or distributor of the product concerned. If the product infringed a provision of the *Food and Drugs Act* or its

Regulations, or any other legislation administered by the Health Protection Branch, its removal was called a "recall." If no statutory infringement was involved, the removal was called a "product withdrawal" or, if the product had not yet been placed on the market, a "stock recovery." The *Food and Drug Regulations* required a manufacturer, distributor, or importer that began a recall to submit certain information to the Health Protection Branch immediately, including the quantity of the drug distributed, the reasons for initiating the recall, and a description of any other action taken with respect to the recall. Neither the *Act* nor its *Regulations* authorized the Department of National Health and Welfare to order the recall of even patently defective or hazardous products. The statutory powers of the Health Protection Branch to respond to the presence of hazardous drugs in the marketplace were limited to the seizure and detention of any drug believed on reasonable grounds to contravene a provision of the *Act* or its *Regulations*; to the cancellation or suspension of the licence issued in respect of a drug listed in Schedule D; or, in the case of drugs for which the government's authorization (a notice of compliance) was a precondition to lawful distribution in Canada, to the suspension of that notice.

In May 1984, the Health Protection Branch distributed to drug manufacturers and others a document entitled "Product Recall Procedures." The document began:

Recall is an effective method of removing or correcting violative products that may represent a health hazard to the consumer or user. It is an action taken by a manufacturer, distributor, or importer to carry out their responsibility to protect the public health and well-being.

During recalls, the primary role of the Health Protection Branch is to closely monitor the effectiveness of the firm's recall actions and to provide scientific, technical and operational advice. If a recalling firm's performance is deemed to be inadequate, the Branch is prepared to take appropriate action to remove the product from sale or use.

The product recall procedures prescribed in detail the "responsibilities" of a manufacturer conducting a recall. The assistant deputy minister, in an accompanying letter, said the procedures were also "currently being used by the Health Protection Branch to facilitate our internal recall responsibilities." The assistant deputy minister encouraged the industry to accept the procedures "as a basic guideline for the recall of foods, drugs, cosmetics and devices" subject to the provisions of the legislation administered by the branch. He added: "There is no intention to promulgate these recall procedures into regulations." Although the procedures did not have the force of law, the branch expected the industries it regulated to comply with them voluntarily.

Apart from the requirements for information, there are still no regulations governing the recall or withdrawal of hazardous drugs. Nor does the Act or its *Regulations*, although extensively amended, empower the Health Protection Branch to order the recall of potentially dangerous products.

The limited resources of the Bureau of Biologics

Approximately thirty persons were employed by the Bureau of Biologics at its inception in 1974. Of these, between twenty and twenty-five were scientists or laboratory technicians. The number of biological products subject to review, licensing, and other regulation by the bureau increased considerably between 1974 and 1982, and many of the new products were blood derivatives. The introduction of a new range of blood products, particularly the coagulation factor concentrates, was acknowledged through the creation in the late 1970s of a separate unit within the bureau, the Blood Products Division, devoted to the regulation of plasma derivatives and other blood-related products. All the positions for which funding had been authorized in the new division, with the exception of the division chief, were eliminated before they were filled because of departmental budgetary restrictions. The division did not have its own laboratory facilities until 1981.

In 1978, as a result of amendments to Schedule D and the *Food and Drug Regulations*, the bureau began to regulate the collection of plasma by plasmapheresis. Its expanded regulatory activities strained the limited resources of the bureau. In early 1977, the bureau's facilities had been described as "grossly inadequate" by a committee established by the Canadian Medical Association and Connaught Laboratories Limited to investigate Connaught's operations. The committee also said that "[m]ore space must be made available and the number of staff increased so that effective control of all biologicals used in Canada may be established." Its report contained twelve recommendations, two of which were directed to the Bureau of Biologics in which, it said, rested the "responsibility for the safety and potency of biologicals used in Canada." One of these recommendations was that research be given a high priority at the bureau. The second read as follows:

The inadequacies in number of staff, laboratory space and animal facilities at BOB [Bureau of Biologics] must be corrected. The increase in staff must be sufficient to enable adequate site inspection of all facilities providing biologicals for Canada and to enable adequate laboratory control procedures to be carried out.

At least partly as a result of the committee's report, the bureau was granted more space, equipment, and personnel. The number of staff positions allotted to the bureau grew to fifty-three by 1982. Five of these positions were assigned to the Blood Products Division, although only four were then filled.

The scope of the bureau's regulatory activities was expanded as a result of amendments to the *Food and Drugs Act* in 1982, further taxing its resources. The number of new biological products, including those resulting from genetic engineering, increased every year between 1982 and 1992. Many of the new products were plasma derivatives or, beginning in the early 1990s, recombinant substitutes for them. Additional pressures developed with the emergence of AIDS. The resources allocated to the bureau through the 1980s did not keep pace with these demands. In 1984 the bureau was authorized to employ fifty-five persons, only two more than before it was recognized that AIDS could be transmitted through blood. Seven of these positions (two of which were unfilled) were in the Blood Products Division. The number of personnel authorized for the bureau grew to fifty-eight in 1987; of these, nine positions (two of which remained unfilled) were in the Blood Products Division. Authority over the collection of whole blood and blood components – in effect, regulatory control over the entire operation of the blood transfusion service of the Red Cross – was added to the bureau's functions in 1989. The full complement of the bureau in 1992, when Dr Furesz retired as director, included only ten more persons (including clerical and administrative staff) than in 1982.

The bureau was unsuccessful throughout the 1980s in its efforts to secure the level of funding needed to discharge its functions effectively. In mid-May 1983, for example, Dr Furesz wrote to the director general of the Drugs Directorate, in part as follows:

The Canadian Regulations [to the *Food and Drugs Act*] pertain to human plasma collected by plasmapheresis and are *not* relevant to collection of *whole blood* or pre-transfusion testing. Although the need for the regulatory control of [Red Cross] Blood Transfusion Services was recognized by this Branch and the Canadian Red Cross (CRC) a number of years ago, due to financial restraint this Bureau is unable to extend its control activities to the entire operation of the CRC. [Emphasis in original.]

The inadequacy of resources not only limited the bureau's ability to extend its regulatory reach, but also affected its performance of the regulatory functions that were directly within its authority. The bureau recognized that adequate regulation of the plasmapheresis program required routine physical inspections of the plasmapheresis centres operated by the Red Cross and private corporations. Although the frequency of the inspections was a matter of discretion, the bureau scheduled on-site audits every two years. However, because of competing demands for limited resources, four years often elapsed between inspections; in the case of one of the Red Cross's centres, the interval was eight years.

The bureau's employees inspected not only plasmapheresis centres but also – and of at least equal importance – the production facilities and operations of the manufacturers of all biological products authorized for sale in Canada, including blood-derived products. During the inspections, the bureau could examine the manufacturer's records related to the production, efficacy, and safety of the biological drugs the bureau had approved for sale in Canada. Dr Furesz testified that such inspections were "a very important part of our regulatory activities" and, "because the procedures are much more complex than any other pharmaceutical manufacturing procedure," required an expertise that was not available elsewhere in the Health Protection Branch. The bureau's policy was to inspect Canadian firms annually, U.S. facilities every two years, and overseas facilities once every three years. This schedule was never followed. In February 1986, for example, Dr Furesz reported to the director general of the Drugs Directorate that "[d]ue to the recent cutbacks on funds and shortage of staff the planned inspections for 1985–86 were only 40% completed."

Regulatory control of the Red Cross blood transfusion service

Financial constraints played a role in delaying the decision to extend regulatory control over the entire operations of the blood transfusion service of the Red Cross – and then in delaying the implementation of that decision. Financial considerations, however, only partly explain why most of the Red Cross's operations remained outside the regulatory ambit of the Bureau of Biologics until late 1989.

Throughout the 1980s, the Red Cross was the only pharmaceutical corporation in Canada that was essentially self-regulated. The Bureau of Biologics and the senior management of the blood transfusion service routinely exchanged information and, beginning in 1981, held scheduled meetings to discuss issues of mutual concern. Starting in late 1984, Dr Furesz regularly attended the semi-annual meetings of the blood transfusion service's advisory committee as an invited observer. Beginning in 1984, Dr Boucher attended most meetings of the advisory subcommittee to the Canadian Blood Committee, at which the activities of the Red Cross were routinely discussed. Dr Furesz testified: "We were still aware of what the Red Cross was doing. We had contact with them. But it was not as good as if they would have been licensed. There is no question about that."

Plasma collected by plasmapheresis ("source plasma") amounted to only 2.5 per cent of the plasma sent to fractionators by the Red Cross in 1982 for processing into blood products, including the factor concentrates used by hemophiliacs. The proportion rose to 6.3 per cent by 1985, but more than 90 per cent of the Canadian plasma used in the manufacture of factor concentrates and other plasma derivatives was still recovered from whole-blood

donations. The components derived from the same whole-blood donations served the needs of all Canadians for transfusions. None of these whole-blood donations – approximately one million donations a year – was regulated by the Bureau of Biologics or any other regulatory agency. In a paper written in 1985, Dr Furesz and Dr Pope commented on the bureau's recently acquired authority to license and regulate the Red Cross's plasmapheresis operations:

This function presents something of an anomaly because plasmapheresis is conducted largely in the same clinics that are responsible for collection of whole blood yet that collection of whole blood is not licensed at the present time. This position is not defensible and there is every expectation that collection of whole blood will eventually be licensed also.

The actions of the Bureau of Biologics

The Red Cross welcomed, and in time encouraged, proposals to extend regulatory control to the collection, storage, and distribution of whole blood and blood components. A task force had been established in the Drugs Directorate in 1980 to select the criteria to be used in selecting drugs for control by licensing and to recommend which drugs should be regulated by the Bureau of Biologics. The task force reported on 23 May 1980 that it "found the current regulation of blood and blood products confusing. The collection and handling of these products is intricate and needs many controls to safeguard the health of donors and of recipients." Because the task force had no evidence of any problem with respect to the unlicensed collection of whole blood by the Red Cross, it made no recommendations about the matter.

Dr Furesz, in a memorandum dated 5 June 1980, responded to the director general of the Drugs Directorate. He said, in part:

Although the Task Force has made no recommendation regarding the licensing of that part of the Red Cross operations that are not currently licensed, we feel that those operations should be subject to scrutiny by an independent agency. Nowhere else in the drug industry is a manufacturer permitted to operate without some sort of independent scrutiny. We suggest that all blood donor operations and products obtained therefrom be licensed whenever such a move becomes feasible.

Dr Furesz testified that by "independent agency" he meant the Bureau of Biologics. He also said that, at the time, the bureau "did not have any concrete evidence to say, 'We do not have any confidence in the Red Cross.'" Dr Furesz was not asked to conduct an assessment of the Red Cross's operations after the task force reported, and the bureau did not conduct an assessment on its own initiative.

The bureau could not subject the Red Cross to its regulatory authority arbitrarily, nor could the Drugs Directorate secure the necessary legislative amendments to achieve this end without ministerial approval. The Red Cross was a highly respected institution. It enjoyed a well-earned reputation for integrity and selflessness based on its long history of public service and humanitarian relief work. Extending regulatory control over its blood services was a question of policy that required careful consideration by the most senior members of the Department of National Health and Welfare. The special status of the Red Cross is reflected in a confidential memorandum dated 28 May 1980 from the director general of the Drugs Directorate to the assistant deputy minister in charge of the branch. In the course of endorsing a Red Cross plan to build a fractionation plant, the director general wrote:

Due to the “special stature” of the Red Cross Society in Canada, the Health Protection Branch has adopted a “hands-off” approach to its operations. This new orientation [towards a fractionation plant] will require that we discontinue this policy and institute normal regulatory procedures. We believe that there will be no objection by the Red Cross to this change in policy.

Dr Furesz expanded on this theme during his testimony, as follows:

[W]e are touching upon the question why the plasmapheresis part of the Red Cross was regulated ... and why did we not regulate the whole Red Cross in 1978. Obviously the financial part is one side of it, but there is another side of it, too.

The Red Cross had a history of about forty years or more as a voluntary agency, non-profit organization, which did a superb job for many, many years. And they were ... a self-regulatory agency at that time. The [Health Protection] Branch, not only the Bureau [of Biologics], the whole Branch recognized the importance of that. The Red Cross had an international reputation at the same time as well. So it was not the highest priority for the Branch in 1978 and even later to expand this [regulatory control].

Dr Furesz said that during the late 1970s and early 1980s, the bureau felt “no pressing need” to regulate blood collection as urgently as – with hindsight – it might seem desirable to have done. Dr Pope described the difficulties involved in extending regulatory control, as follows:

What we had was a bureau which was loaded up to the gunnels with jobs to do and responsibilities, and [it] was operating and coping. That was one aspect. Another aspect was there [were] more jobs to do, and the Red Cross is a good example of where there was a need for additional

regulation and control because a cottage industry was growing up and we now had an institution which outclassed in size any drug company that exists in this country.

We have just successfully managed [in 1978] to regulate plasmapheresis, but look at the obstacle: do it on your own with the resources that you have at the moment. And that was what the Bureau did.

The picture facing any move on our part, or thrust on our part, to be able to cope with taking over of the regulation of this huge organization, quickly and simply, was not very optimistic. What we would have to do is to get concurrence from the highest level of the departments. My opinion is that it is way up above the [Health Protection] Branch level, that this is the Minister's level, and that he may even be taking the thing through to Cabinet.

The extension of regulatory control over the entirety of the Red Cross's blood program was also complicated by the participation of the provincial governments in the Canadian blood system. Adding "blood" to the schedule of drugs subject to regulation by the Bureau of Biologics had financial implications for the operation of the blood transfusion service and consequently for the provinces, because they paid for the service through the Canadian Blood Committee. It was not until the mid-1980s that the committee acknowledged the advantage of external regulation of the entire blood transfusion service. That acknowledgement came about as a result of an increasing appreciation of the risk of the transmission of AIDS through transfusion and following the committee's discovery – during a visit to the Red Cross's national reference laboratory – of what it characterized as "deficiencies which could constitute health hazards."

In a "briefing information" to the assistant deputy minister dated 19 March 1985, the Bureau of Biologics recommended that it be given the authority to regulate all the activities of the Red Cross blood transfusion service. In this document the bureau summarized the reasons for its recommendation, as follows:

Background:

- Presently the BTS [blood transfusion service] is a very large, nation-wide operation run by 17 regional collection centres operating under general direction of the central offices of the CRC [Canadian Red Cross]. Blood is collected, processed into various products and distributed to hospitals throughout the country. The CRC claims that the operation is larger than all of the members of the Pharmaceutical Manufacturers Association of Canada put together.
- The Canadian Blood Committee, following inspection of some of the BTS facilities, has urged that the CRC BTS be required to meet the same standards as any other drug manufacturer.

- The CRC recognized the deficiencies discovered by the Canadian Blood Committee and has requested additional funding to upgrade its operations in anticipation of having to be licensed by the Health Protection Branch.
- Health risks attributable to unsatisfactorily collected and processed blood products are serious, including transmission of hepatitis and AIDS ...

Current Status:

- The World Health Organization requires that blood collection and processing be regulated by the National Control Authority.
- In the U.S. and Britain, blood is considered a biological drug and all facilities involved in blood collection are licensed accordingly.
- Although the Bureau of Biologics took several important initiatives in the past seven years ... the Bureau does not have the resources to expand its regulatory activities to the entire Red Cross blood collection operation.

Suggested Departmental Position:

- Provision be made for additional resources ... for the Bureau of Biologics to conduct inspections of BTS centres, review and validate blood transfusion procedures and test blood and blood products.
- This action is necessary as each year BTS collects over one million blood donations, each of which may be used in four or more patients. The lack of regulatory control of premises, collection and processing procedures, could result in health risks not only for the healthy donors but for the millions of patients who receive this life saving drug.

Dr Furesz testified that this briefing information could not have been worded more forcefully. It described a significant risk associated with the donations collected at the blood centres. That risk could not be dealt with by the bureau until it had appropriate legal authority. It sought the legal authority and the resources necessary to exercise that authority. As Dr Furesz testified, "without resources there is no authority."

It was not until September 1989, four and a half years after its request to the assistant deputy minister, that the bureau obtained the authority and resources required to regulate the collection of blood. In the interim, members of the bureau communicated with their superiors about the proposal but did not press it with sustained vigour. In hindsight, Dr Furesz agreed, it would "have been prudent to write another memo and said, 'This is getting more urgent with every passing day.' "

There were no fresh representations to extend the bureau's regulatory authority over the Red Cross until mid-1987, and then they were made primarily as a response to proposals by private entrepreneurs to establish commercial blood banks. These commercial initiatives caused Dr Furesz to write, in a memorandum to Dr Boucher dated 5 May 1987, that "the time has arrived

for putting ‘Blood’ on our schedule.” Within days, the bureau had drafted a formal “justification” for its proposal that blood be added to Schedule D of the *Food and Drugs Act*, “thus permitting licensing of blood transfusion services and blood banks.” The “background” to the proposed amendment read:

- Schedule D lists those drugs that are subject to licensing and extra controls authorized by Section 12 of the Food and Drugs Act.
- The Canadian Red Cross (CRC) Blood Transfusion Service is upgrading its operations to meet the requirements of the Food and Drugs Act.
- The CRC has been the only organization operating blood banks and transfusion centres in Canada but, now, private commercial organizations are proposing to set up alternative services. Individuals will be able to donate blood for their own use (autologous transfusions) so as to avoid perceived risks of contracting diseases that could be transmitted by transfusion of blood from unknown donors.

Dr Furesz’s memorandum said that the Red Cross had “already asked the Minister to license its transfusion centres” and that one commercial operator and the promoters of others had been made aware of “their need to comply with standards necessary for a licence.” The “health and social” justification for the proposal was described as follows:

- Manufacture of drugs of biological origin such as blood and blood derivatives has high potential for harm unless especially rigid standards are observed.
- Licensing of CRC will ensure continuing future compliance with the highest standards of good manufacturing practices.
- New, commercial blood banks have potential for even greater hazards unless there are controls to ensure they maintain required standards.

The memorandum concluded by saying:

- Control of emerging commercial blood banks is urgently needed. Because of their small number departmental resources do not need to be increased for this action. Licensing of CRC facilities will have to be delayed until they have been satisfactorily upgraded but, once operational, [additional] departmental resources will be required.

The bureau’s plan to delay regulatory management of the Red Cross’s blood centres “until they have been satisfactorily upgraded” was impracticable because the inclusion of “blood” in Schedule D would necessarily subject the Red Cross to the same licensing requirements as those imposed on commercial blood collectors. The bureau had only enough employees to oversee the activities of a few new commercial facilities. In a memorandum dated

5 June 1987 to the director general of the Drugs Directorate, Dr Pope said that the “[a]ddition of ‘Blood’ to Schedule D, providing authority for enforcement, is being delayed because immediate licensing of *all* transfusion centres will be required once that addition is made.” The emphasis was Dr Pope’s. The bureau did not obtain the authorization to increase the number of its employees, however. In the memorandum of 5 June 1987, Dr Pope said that “[r]esources for licensing blood transfusion centres have to be found in the existing [personnel] base,” but because staff members could not be diverted from other essential regulatory tasks, the bureau “is unable to license blood transfusion centres by using resources from its existing base.”

Coincidentally, the day before Dr Pope wrote his memorandum, Dr Denise Leclerc-Chevalier, the executive director of the Canadian Blood Committee, raised the same issue in a memorandum she sent to the assistant deputy minister in the Department of National Health and Welfare, who represented the department on the committee. She wrote:

In your discussion with our Deputy Minister, Dr. Law, in relation to the Canadian Blood Committee, I would appreciate it if you would raise the issue of the need for the Bureau of Biologics to take action on licensing of Red Cross facilities and private industry facilities, development of standards for blood and blood products and blood substitutes.

There is a lack of personnel in the Bureau of Biologics to deal with blood and blood products and I feel that the federal government is not playing its role of “protecting the population against health hazards relating to drugs, more specifically biologicals.”

By June 1987, in short, the Red Cross, the Canadian Blood Committee, and the Health Protection Branch had recognized that the Red Cross’s blood transfusion service should be regulated, but the branch lacked the resources to be able to do so. More than two more years would pass before “blood” was added to Schedule D of the *Food and Drugs Act*, in September 1989. Dr Pope testified, “I do not know whether we [the bureau] could have done much more.”

The response of the senior management of the Department of National Health and Welfare

Officials at more senior levels of the Department of National Health and Welfare did not have the same appreciation as the Bureau of Biologics of the value of extending federal regulation to the collection and processing of blood. Dr Furesz was routinely in contact with the Red Cross about the blood system and, drawing on his experience, proposed the extension of regulation. Others in the department were not persuaded that the situation required adding to the “regulatory burden” or, if so, whether provincial

measures were not more appropriate. During the early and mid-1980s the political climate favoured deregulation and, except in the clearest of cases, the executive was unsympathetic to new regulation. Extending regulatory authority to the blood transfusion service of the Red Cross required, as a precondition, a regulatory impact assessment and a demonstration that the necessary expenditure of funds would result in a net increase in public health that could not be achieved by some more modest or alternative means. There was no need perceived for federal regulation if the safety and quality of the Canadian blood supply could be maintained without it.

Mr David Kirkwood served two ministers of National Health and Welfare as deputy minister from 1983 until 1986. During his tenure, the issue of the department's regulatory authority over the Red Cross was never raised by his ministers, nor did the Health Protection Branch, the Drugs Directorate, or the Red Cross ever ask him to endorse and transmit a recommendation to either minister to regulate the Red Cross.

Significant amendments to the *Regulations* required careful planning, approval of funding, and the availability of appropriate personnel and facilities. "Multi-year operational planning" initiatives of this type would normally take about five years. Drafting and enacting new regulations alone often took more than a year. A purely technical amendment involving no more than the addition of a single drug to a statutory schedule could be accomplished in a few days. The inclusion of "blood" in Schedule D to the *Food and Drugs Act* was much more complicated because of the political implications. As Mr Kirkwood explained:

I don't think the proposal to extend the regulation of blood products to apply to whole blood collection would have been considered a simple technical issue because it would have involved a substantial change in the relationship, if that is the right term, between the federal Department of Health and Welfare and the Red Cross. And as I have said earlier, the Red Cross was perceived as being in a sense the creature of the provinces in the sense that it was funded by the provinces and received its direction from the Canadian Blood Committee which was, in effect, an inter-provincial body with a federal representative present holding a watching brief. To regulate directly the blood collection activities of the Red Cross would have involved substantial changes that would, I am sure, have required extensive discussion with the minister because of the political implications for his relations with his provincial counterparts ...

I would offer the suggestion that extending the regulatory requirement would probably involve the Red Cross in a significant increase in costs, or at least could so, and that would have an impact on the provinces since they fund the operation.

Dr Albert Liston held senior management positions within the department for almost two decades. He was appointed director general of the Drugs Directorate in 1974, executive director of the Health Protection Branch in 1981, and assistant deputy minister in 1984, a position he held until 1992. Throughout these years, the Bureau of Biologics was under Dr Liston's managerial supervision. Dr Liston had discussed the regulation of the Red Cross with Dr Furesz as early as 1980, but only "as a question of something that should be looked at and given study." No decision had been made to regulate whole-blood collection at that time, nor was this a subject of regular discussion. However, Dr Furesz's memorandum of 5 June 1980, in which he suggested that licensing requirements be extended to all blood donor operations, constituted what Dr Liston called "the beginning of the process of starting ... to actively consider whether regulation of blood should take place."

From the department's perspective, the process was slow because the Red Cross blood collection operations were "under control." The Red Cross had its own expertise and its own standards in place to address potential problems, and it followed the guidelines of the World Health Organization. A significant "additional benefit," which then was not apparent, would have to be demonstrated before an extension of regulatory authority could be seriously considered. Dr Liston testified that, eventually,

[t]here started to be requests from the Red Cross that were made through the Bureau of Biologics for blood to be regulated, and during a period of time, this question of who and how should it be regulated was one which the department addressed. I know the Deputy Minister of Health looked at this and felt that we should examine whether or not it was more appropriate for the provinces to regulate it or to control it as opposed to the federal government, or the health department, or more specifically HPB [the Health Protection Branch] ...

The question ... is were the procedures, call it the self-regulation, was it adequate or would there be incremental benefits which would accrue to public health if it was regulated?

Dr Liston was aware that the Red Cross would welcome the regulation of blood collection. For the Red Cross, regulatory control would enhance its quality assurance, add a measure of certification to its operating procedures, improve its position in its financial negotiations with the Canadian Blood Committee, and offer some degree of liability protection through regulatory compliance. For Dr Liston, however, the Red Cross's desire to be regulated was "not necessarily a compelling argument for going ahead to regulate." There was nothing preventing the Red Cross from improving the quality and safety of its operations by itself; it did not need an external regulator, for example, to prepare its own standard operating procedures and apply them throughout the blood transfusion service. Regulation may have limited the

Canadian Blood Committee's ability to deny the Red Cross the funds required to ensure compliance with the regulations, but this again was "not necessarily a compelling reason for regulation."

Dr Liston testified that Dr Furesz's proposal in 1985 to regulate the collection of blood "may not have competed favourably with other higher priorities within the Health Protection Branch." Competing demands within the department included developing a Canadian technological base in the pharmaceutical industry, reducing the backlog of new drug submissions, responding to concerns about acid rain, providing adequate health care services to native people, and ensuring the safety of pesticides. There were "human crises in many of these areas," said Mr Kirkwood, all of them striving for "a shrinking pool of resources," and "[t]o increase the resources in one area at a time when overall allocations had to be reduced meant doubly penalizing some other area, both because of the general cut and because something had to be transferred out."

In short, it was difficult to obtain additional resources, and regulation could not be implemented without the necessary resources. Dr Liston testified that through much of the 1980s, the political and fiscal reality was that existing resources would have to be used if the bureau was to regulate the collection and distribution of blood. Mr Kirkwood testified that ultimately the case had to be made at the policy, or ministerial, level. Although the Treasury Board's secretariat controlled federal expenditures, "if the Minister had previously gone to Cabinet and obtained Cabinet approval, the Treasury Board would ... scarcely be in a position to say, 'Despite the policy decision, we're not prepared to allocate funds.'"

Dr Liston summarized the process by which the policy decision to extend federal regulatory control to blood collection in 1989 was finally made:

Through the period of the eighties ... there was progressively more activity in this area, and a decision was made to proceed with the regulation of blood because it would offer some incremental benefits and it would respond to a need to regulate anyone else who might come into the blood collection domain. So there was a decision. It was not predicated on a crisis situation which had necessitated an immediate regulatory intervention.

The proposed amendment to Schedule D that added "blood" to the list of drugs subject to the authority of the *Food and Drug Regulations* was published in the *Canada Gazette* on 23 March 1989. The purpose of the amendment, as described in the accompanying regulatory impact analysis statement, was "to ensure that quality assurance programs are in place for blood used by Canadians." The statement continued:

The benefit to public health is the avoidance of an infectious disease. As we are aware, these diseases require expensive drugs, extended

hospitalization, and cause a decrease in the quality of life. The public health care system will benefit by ensuring that blood is manufactured under conditions and in premises that minimize the risks associated with these drugs, thereby reducing the public tax burden for health care.

These "added safeguards" were found to outweigh the costs of regulatory control, thus justifying the proposed amendment.

The bureau's use of its regulatory authority

The regulatory authority of the Bureau of Biologics was restricted to the drugs listed in Schedule D to the *Act*. "Blood derivatives," the term that in 1982 replaced "sera and drugs analogous thereto" in the schedule, could be interpreted to include recovered plasma and blood components, both of which are derived from blood. However, this is not how the term "blood derivatives" was then understood among persons who collected and processed blood and manufactured blood products, or among those who regulated these activities. "Blood derivative" was, in effect, a term of art. Products manufactured from plasma were within its compass. Whole blood and blood components, such as red cells and recovered plasma, were not.

Even though "blood" fell outside the scope of the bureau's regulatory authority in the 1980s, there were measures available to the bureau to enhance, however marginally, the safety of both the plasma from which factor concentrates were custom fractionated for the Red Cross and the components used for blood transfusion.

The plasmapheresis provisions, which were added to Division 4 in 1978, required that the donors of source plasma be interviewed and evaluated to ensure that they were free from infection, any disease that created a risk of contamination of the plasma, and any blood-borne disease. By September 1983, the bureau was aware that at least one Canadian commercial plasmapheresis operator had implemented a procedure to detect and defer prospective donors who had AIDS or AIDS-related infections or were at high risk of exposure to AIDS. All the source plasma that went into the plasma pools that were custom fractionated into factor concentrates used by Canadian hemophiliacs was collected by the Red Cross. The Red Cross had its own procedures to evaluate the health of its plasmapheresis donors. In 1983 and 1984, these procedures did not include the use of questions or other measures designed specifically to detect persons at risk of contracting AIDS. The bureau knew this. It also knew it had the authority – which it did not exercise – to require the Red Cross to amend its plasmapheresis procedures to include AIDS-sensitive questions and measures.

The bureau could also have invoked the provisions governing "preparations from human sources" to require the manufacturers of factor concentrates to ensure that the plasma they used as source material was as free as possible from contamination with AIDS. To meet this condition, the manufacturers

would then have required their plasma suppliers to satisfy them that they were actively screening donors. Measures of this nature were implemented, beginning in late 1982, by centres collecting blood and plasma in the United States, which supplied roughly half the plasma needed to meet the Canadian demand for blood products. The other half was supplied by the Red Cross, which did not begin to introduce any AIDS-related donor deferral procedures at its blood centres until mid-1984.

Because most of the plasma collected by the Red Cross was recovered from whole-blood donations, any measures that reduced the risk of HIV contamination of the custom-fractionated plasma pools would necessarily have enhanced the safety of the components used routinely for transfusion purposes throughout the country. A timely policy directive from the bureau, in reliance on its authority to regulate the safety of preparations from human sources, would have compelled the custom fractionators to require the Red Cross to screen donors for AIDS or for possible exposure to AIDS. The safety of custom-fractionated concentrates and transfused components could similarly have been enhanced had the bureau exercised its authority to impose the implementation of AIDS-sensitive donor screening as a condition for the maintenance of a manufacturer's licence.

Until 1989, when "blood" was added to Schedule D, the Red Cross was not permitted to distribute blood unless it had been produced in accordance with the regulations governing good manufacturing practices. Among other things, these regulations prescribed the testing of raw material and finished products against detailed specifications; manufacturing and quality control; the institution of rapid recall procedures; and the maintenance of comprehensive records. The Health Protection Branch, either through its Drugs Directorate or its Field Operations Directorate, had the authority to enforce these regulations at the Red Cross blood collection and processing centres. It did not do so.

The Public Health Environment

Public health officials, as the term suggests, work to prevent the spread of disease and to promote and protect health in their communities. In their concern for large groups of persons they differ from most physicians and other health care workers, who focus on the treatment and care of individuals and their families in clinics or in hospitals. Public health officials are expected to be aware of developments in medicine and science, including the emergence of new diseases in their own and other communities; to monitor the occurrence of diseases in their communities; to advise governments about policies relating to health; and to provide information to health care workers, physicians, the general public, and groups who may be at high risk of contracting a particular disease. They may work at the local, regional, provincial, national, or international level. Many are government employees whose responsibilities are defined in statutes – in Canada, principally in provincial legislation. They do not work alone. Communicable diseases, for example, are most often diagnosed by family physicians or infectious disease experts, who may be required by statute or regulation to report the diseases to the appropriate public health officials. Personal physicians may offer counselling about ways of dealing with the consequences of disease and of preventing its spread to others. At times, social workers and other experts may also become involved. The organization, management, and financing of personal health care and public health services are quite distinct, but they are interdependent. The effectiveness of any public health program depends largely on effective communication with other public health agencies, with physicians and other health care workers, and with the residents of the community.

Preventing the spread of infectious diseases, irrespective of their means of transmission, is a significant task of public health authorities. Both the collection and the use of blood and blood products can be a means of transmitting infectious diseases that affect the health of the public. Public health officials must therefore be concerned with diseases, and especially new diseases, that may be transmitted by blood.

In Canada, jurisdiction over health matters is shared between the federal and the provincial governments, but is primarily a provincial matter. The *Constitution Act, 1867*, grants the provinces legislative authority over local

matters, property and civil rights in the province, and the establishment, maintenance, and management of hospitals, except for marine hospitals. Disease prevention, health education, and treatment of disease are thus subjects within provincial legislative jurisdiction. The federal Parliament also has legislative authority over public health through its powers over international and interprovincial trade and commerce, the criminal law, quarantine, the establishment and maintenance of marine hospitals, aboriginal persons, census and statistics, and the residual power in respect of peace, order, and good government. Its criminal law power is broad enough to enable the federal government to cause legislation to be enacted to prevent harm to the health of Canadians and to give it a role in health education and the prevention of disease, including potential harm from blood components and blood products.

Federal public health bodies

In 1982, the federal public health functions were discharged by the Department of National Health and Welfare, and in particular by its Health Protection Branch. There were several such departmental branches, each headed by an assistant deputy minister. The Health Protection Branch assessed, gave advice about, and managed risks to the health of Canadians. It had the tasks of protecting the public against unsafe foods, drugs, and environmental dangers; monitoring the occurrence and causes of communicable and non-communicable diseases; and establishing uniform standards for the diagnostic tests used by laboratories to determine the presence of diseases. Its national health surveillance program was designed to coordinate the identification, investigation, control, and prevention of diseases in Canada.

Two directorates in the branch were of principal importance in Canada's response to the threat to public health from AIDS. One was the Drugs Directorate, in which was situated the Bureau of Biologics, the regulator of blood and blood products. The second was the Laboratory Centre for Disease Control. The Bureau of Biologics is discussed in Chapter 6.

Laboratory Centre for Disease Control

The services of the Laboratory Centre for Disease Control were available to the provinces. It gave advice and information to provincial departments or ministries of health, and assisted in the diagnosis of communicable diseases to help them to identify threats to health and to react to identified threats. It also had a surveillance role, monitoring public health and emerging diseases both nationally and internationally. More specifically, its tasks included

- epidemiological, laboratory surveillance, and diagnostic systems for disease control;
- national programs for microbiological reference centres, quality assurance systems, and laboratory medicine; and
- national programs for infection control in laboratories and hospitals.

The centre analysed provincial and national data and reported the results in the *Canada Diseases Weekly Report*, which had a distribution of 10,000 copies and was sent without charge to provincial epidemiologists and medical officers of health.

In the centre, three bureaus were of special importance in preventing the spread of blood-borne communicable diseases. The Bureau of Infection Control, established in 1980, gave advice about the control of community-acquired infections and developed national programs for the control of infections acquired in laboratories and hospitals.

The Bureau of Microbiology conducted research into problems of public health and gave information, advice, and training to provincial public health officials with respect to infectious diseases. It offered diagnostic reference services, including the culture and identification of microorganisms in clinical specimens sent to it by provincial public health officials or university and hospital laboratories for the diagnosis of patients. It also developed methods for the early, rapid, and reliable detection of established and emerging infectious diseases – including the production and distribution of reagents, materials used in tests for infectious diseases – that were not available commercially. It assisted the provinces in evaluating their own technical staff, made available training and manuals in the diagnosis of infectious diseases, and helped to investigate outbreaks of diseases. It also operated national reference centres for hepatitis, gonorrhea, meningitis, rickettsia, and food-borne infections. Federal funding supported reference centres for some other infectious diseases in provincial laboratories and universities; for example, the Public Health Laboratory in Edmonton had a diphtheria reference centre, and McGill University had a reference centre for parasitic infections. If Canada lacked expertise in a particular infectious disease, inquiries were referred to specialists outside the country, such as those at the Centers for Disease Control in Atlanta, Georgia.

The Bureau of Epidemiology was concerned with both communicable and non-communicable diseases. It developed national surveillance programs and analysed the occurrence of particular diseases based on the data it received from provincial public health officials. It also studied and evaluated data about diseases in hospitals, laboratories, communities, and internationally, and it established policies to control diseases, including imported and exotic diseases. Its interests included biological markers that could be used in tests to identify the presence or probable presence of specific diseases. The Bureau of Epidemiology collected information about adverse reactions to drugs and vaccines. It did not collect information about adverse reactions to blood components and blood products. Under a special program created in 1975, it sent field epidemiologists to assist local epidemiologists in dealing with outbreaks of disease, among them listeriosis in Nova Scotia in 1981, suspected cases of Lassa fever in Toronto in 1976, and hemorrhagic E. coli ("hamburger

disease") in the early 1980s. Federal field epidemiologists were also available for continuing and special provincial projects. The bureau had four field epidemiologists, who were employed for terms of two years.

Advisory Committee on Epidemiology

The Department of National Health and Welfare established an Advisory Committee on Epidemiology in February 1962 as a forum for the "regular consultation and co-ordination of effort" of federal and provincial public health officials and as a forum for the exchange of information about emerging infectious diseases. The committee was empowered to

discharge, carry out and perform such duties, powers and responsibilities as are necessary to assist and advise the Minister on matters relating to the study, prevention and control of disease in Canada ... and without limiting the generality of the foregoing, the Committee and any Subcommittee thereof may make special studies, examinations or investigations, consult with such persons as may be necessary and generally to do all acts, matters and things as will lead to the best development in Canada of the epidemiological study, prevention and control of communicable and non-communicable diseases.

The committee met annually. Before 1982 it discussed, among other matters, the field epidemiology program, diseases that should be made notifiable by the provinces, a Canadian contingency plan (a coordinated response to communicable disease emergencies), and the management of such diseases as hepatitis B, measles, and Reye's syndrome.

A frequent topic of discussion after 1978 was the inadequacy of the committee's reporting relationship with ministers of health and senior public health officials. The committee did not report directly to the federal deputy minister of health. It reported instead to the Federal-Provincial Advisory Committee on Community Health Services, one of six federal-provincial advisory committees established by the Conference of Deputy Ministers in 1977. It was often difficult to place epidemiological issues on the agenda of the federal-provincial advisory committee. Some provincial epidemiologists complained in 1978 that the reporting relationship obstructed cooperation, coordination, pooling of resources, and sharing of activities among provinces. Dr Alastair Clayton, the director general of the Laboratory Centre for Disease Control, who chaired several meetings of the Advisory Committee on Epidemiology, described the relationship as frustrating. When the committee met in 1981, Dr Clayton reported that he had recommended to the assistant deputy minister responsible for the Health Protection Branch that a new federal-provincial advisory committee on communicable disease control be

created. He said that his recommendation was unlikely to be accepted, however, because senior federal health officials were reluctant to broaden the existing federal-provincial committee structure.

The Advisory Committee on Epidemiology did not discuss the subject of AIDS until May 1983, nearly two years after the *Morbidity and Mortality Weekly Report*, published by the U.S. Centers for Disease Control, reported that five seemingly healthy homosexual men in the United States had contracted *Pneumocystis carinii* pneumonia, suggesting "the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections such as pneumocystosis and candidiasis," and fourteen months after the *Canada Diseases Weekly Report* reported that a homosexual man in Canada had died of the same disease. In his testimony, Dr Clayton said that the committee's delay in considering AIDS was because "[i]n comparison with other issues that were relevant in communicable diseases, it was not the biggest one ... it was certainly overshadowed by many other diseases." At that time, several provincial epidemiologists believed that AIDS would be confined to the United States, that it would not become a problem in Canada, and that other diseases should be given a higher priority.

Provincial public health authorities

A department or ministry of each of the ten provincial governments was devoted to health matters in 1982. Although the organization of the department varied throughout the country, it usually included a minister of health, a deputy minister, one or more assistant deputy ministers, and directors of branches or divisions in the department. One section of the department was normally given the task of dealing with public health, the monitoring of the occurrence of disease, and the taking of preventive action to protect the health of the residents of the province.

Provincial public health services

Although most of the provincial functions and duties in respect of public health were delegated to regions or municipalities, the Minister of Health was the ultimate authority. The ministerial powers varied, but were often broad. For example, in New Brunswick, subject to the approval of the Lieutenant Governor in Council, the Minister could make such rules, orders, and regulations as he or she deemed necessary for the prevention, treatment, mitigation, and suppression of disease and the conservation of human health and life, and might, among other things, provide for and regulate

- the management, maintenance, functions, duties, qualifications, and jurisdiction of health districts, medical health officers, and all other officers under the *Act*;
- the prevention, control, and reporting of communicable and other diseases;

- the specifying of certain communicable diseases, and the requiring of medical practitioners attending a person suffering from one of those diseases to notify the district medical health officer for that district;
- the prevention or mitigation of epidemic, endemic, infectious, or contagious disease;
- generally, all such matters, acts and things as may be necessary for the protection of the public health and for insuring the enforcement of the *Act*.

Similarly, the *Department of Health Act* in Saskatchewan specified that the Minister might do whatever he or she considered advisable for promoting the health of the people of the province, and in this regard might

- initiate, promote, conduct and maintain surveys, scientific and administrative research programs, and planning studies into any matters relating to health needs in the province and obtain statistics for purposes of the department;
- collect such information and statistics respecting the state of health of members of the public, health resources, facilities and services, and any other matters relating to the health needs or conditions affecting the public as are considered necessary or advisable, and publish any information so collected.

The section of the provincial department or ministry dedicated to public health policy and programs was usually led by a chief medical officer of health, although the title varied from province to province. This officer reported to the provincial minister of health and ensured that local health units discharged their function. In Prince Edward Island, for example, the regulations under the *Public Health Act* provided that the chief medical officer of health "shall have overall responsibility for the control of regulated disease in the province, including the investigation, management and follow-up of cases and agents of transmission." In Quebec, the head of the community health department was required to take the necessary measures to prevent and arrest contagion or epidemic and to protect the health of a population when told about a reportable disease. Certain diseases, listed in the provincial statutes or regulations, were designated as "reportable" or "notifiable," depending on the province.

Some provinces also had sections or separate centres for communicable diseases. The Vancouver Bureau (later renamed the British Columbia Centre for Disease Control), for example, served as the provincial centre of expertise and made available specialized services to the regions. Staff members at these centres might be involved in research, testing, early diagnosis, immunization, and treatment.

Provincial departments and ministries collected and analysed information in order to monitor the state of health of the residents of their province. Some employed a full-time epidemiologist for this purpose. The information was used to assist in the planning of health care, in operating public health services, and in defining and supporting public policy measures.

Provincial public health laboratories assisted in the identification and control of epidemic and endemic diseases. Some provinces had branch laboratories to assist local health agencies and physicians. The main functions of the public health laboratories were routine diagnostic testing, research, and public education.

Health units

Public health programs in 1982 were administered by health units based on geographical divisions that most often coincided with local administrative units, either municipalities or regions. Metropolitan areas with high population densities had their own health units; some large cities had more than one. Metropolitan Toronto, for example, had four units. Health units formed liaisons with local hospitals, medical practitioners, and voluntary health agencies, and in most provinces had their own buildings and staff. The range of their services was broad; they might include "well baby clinics," sexually transmitted disease clinics, dental hygiene instruction in schools, public education, inspection of restaurants and other food-processing and handling operations, and investigation of environmental and occupational health and safety conditions.

Most health units were directed by boards, which varied in composition and method of appointment. The means of appointment, duties, responsibilities, and authority of the boards were set out in provincial legislation. In some provinces, combined boards were responsible for the administration of public health services in several regions. The health units were publicly accountable to their elected municipal councils and, in some matters, to the province's chief medical officer of health. The goals and minimum standards were determined by the provincial government, and some provinces had mandatory core programs. The boards determined programs and policies for their communities within the limits of the provincial legislation and the funds allocated to them. Essentially, they were responsible for the promotion and protection of health, the prevention of the spread of disease, and the delivery of public health programs and services.

Health units were funded principally by the provinces. In most provinces, local governments allocated additional funds for programs that went beyond the province's mandatory core programs. This additional funding afforded the flexibility needed to assess and meet local needs, but it also contributed to a lack of uniformity in service.

Health units had a medical officer of health, or a person with a similar title, who was a physician and who advised the local board of health, carried out certain duties related to public health, and evaluated the status of the community's health. The statutory duties with regard to communicable diseases varied from province to province, but medical officers of health were expected to investigate all occurrences of notifiable or reportable disease in the municipality or region for which they were responsible; to establish the cause, mode of transmission, and probable source of the disease; and to identify other persons who might be at risk. They were also expected to take whatever steps were reasonably possible to suppress the disease in those who might already have been infected, to protect those who had not already been exposed, to break the chain of transmission to prevent the spread of the disease, and to remove the source of infection. They could compel a person suspected of having a communicable disease to undergo a medical examination by a designated physician, submit a specimen to the public health laboratory for analysis, and undergo prescribed treatment. They had the statutory authority to isolate or quarantine persons who were infected, or suspected of being infected, with a communicable disease. In most provinces, they could also quarantine other persons in sexual or social contact with the infected person.

In order to plan, coordinate, and evaluate community health programs and services, the medical officer of health worked with a multidisciplinary team, including public health nurses and inspectors – the members most often in contact with the public – and collaborated with other health and social service agencies. The medical officer's role was usually that of health administrator and coordinator of community health matters. In some parts of the country, however, the medical officer of health was employed only as a consultant in medical matters, such as the control of communicable diseases and screening programs. The health unit then would be managed by a health administrator.

The board of health was required to ensure that the health unit had enough employees to carry out its responsibilities. The composition of the public health teams varied according to the needs of the particular region and the core programs that were required by the provincial government. Usually the teams included public health nurses, nutritionists, dental hygienists, health educators, inspectors, and engineers.

Notifiable and reportable diseases

In every province, physicians were required to report certain communicable diseases. In most provinces, laboratories that performed diagnostic tests for communicable diseases also were required to report. The lists of diseases varied from province to province, but were for the most part similar. In addition to the specified diseases, the legislation in some provinces contained a general clause about reporting any rare or unusual disease or syndrome, or

any other disease that might endanger the public health. Information about reportable diseases in each province was forwarded to the Laboratory Centre for Disease Control for national collection and analysis.

Physicians and laboratories were usually required to report occurrences of the notifiable diseases to their local public health authority, which sent the information to the provincial department or ministry of health. In some provinces the duty to report was extended to school principals, persons in charge of institutions such as nursing homes and day care centres, and even householders. In most provinces, the physician treating a patient with a notifiable disease was required to report the infection as soon as possible or within a specified period – for example, within twenty-four hours. Provincial forms required detailed information, such as the name, age, and sex of the infected person, and clinical or epidemiological data. All provinces consolidated the data from the regions and transmitted those items that were on a national list to the Laboratory Centre for Disease Control. Summary data appeared in reports issued regularly at both the national and the provincial level.

Although reporting to provincial authorities was mandatory, the data were incomplete. Some diseases were more likely to be reported than others, and some physicians were more likely to report diseases than others. Moreover, diagnoses were not always accurate, and not all provinces required reporting of the same diseases. The data were useful, despite their limitations, for assessing the state of community health, identifying high-risk groups, and evaluating control programs. They were also generally adequate for monitoring trends at the provincial and national levels. The system was restricted, however, to diseases that were specified in statutes or in regulations. As a result, it was not useful for identifying emerging diseases.

The process of identifying an emerging disease

A person who feels unwell usually goes to his or her physician. Many diseases and infections have similar signs and symptoms, and it is often difficult for a physician to make a definitive diagnosis. Until a physician has several similar cases, or has learned of similar cases from colleagues, specialists, or the professional journals, it is unlikely that he or she will recognize that a possible threat to public health exists.

Whether public health authorities are notified of an emerging disease, and, if so, when, depends on a number of factors, the most important of which is the examining physician. If the symptoms are general, it is unlikely that the first cases of the disease will be recognized, reported, or even serve as a trigger for identification. The identification of a new disease is likely to be much faster if it has some distinguishing feature that stimulates the physician to seek additional information, talk to colleagues, or refer the patient to an infectious disease specialist.

The recognition that there is a new threat to public health will probably result from communication among physicians, but, if there are no laboratory tests, signs, or symptoms, or if the disease is unknown, it is difficult to define adequately what constitutes an occurrence of it. If the definition is too specific, new or more unusual manifestations may be missed. On the other hand, if the definition is too broad, it can include the characteristics of many other illnesses, resulting in an inflated view of the new disease's prevalence.

At some stage in the process, either the local public health authorities or the provincial officials involved with disease control will be informed and involved. How the next steps are taken, and by whom, depends on the seriousness of the disease, the ability of the laboratory to identify it, the early indications of the mode of transmission, the extent of the problem, the resources available, and the readiness of public health authorities to act.

An active investigation usually begins with a search for any similar cases that have been identified elsewhere in the province, in the country, or in the world. The work may start locally, but few local health units have the staff or the expertise to devote to a detailed investigation or epidemiological study. It is more likely that the provincial department or ministry of health, in collaboration with the local unit or units involved and perhaps with the help of the Laboratory Centre for Disease Control, will seek to determine the nature and the extent of the problem and any measures that can be taken to contain the spread of the disease, prevent its transmission, or in other ways control the risk. After the initial investigation, epidemiological studies may be conducted and surveillance procedures may be implemented to record occurrences throughout the country. Large epidemiological studies, although of interest to public health authorities, may be initiated and conducted by treating physicians or research scientists, alone or in collaboration with public health officials. Links may also be established with research laboratories where work has begun to identify the causative agent of the disease or to develop tests to detect its presence.

Many groups, organizations, and individual specialists are likely to collaborate in this research. They include hospitals, laboratories, infectious disease specialists, medical officers of health, epidemiologists, provincial and national data collectors and analysts, groups of persons found to be at higher than normal risk of contracting the disease, and organizations that might be affected. Throughout the process, effective communication among all the participants is critical to success.

Public health authorities outside Canada

In their work, Canadian public health officials could draw upon the knowledge and expertise of their counterparts elsewhere. The closest links were with organizations in the United States. They were also kept informed about

advances in knowledge through the formal channels of medical and scientific journals and conferences, and through the network of informal contacts among specialists that is characteristic of all science.

Public health institutions in the United States

The principal national institutions in the United States dealing with infectious diseases were the Centers for Disease Control and the National Institutes of Health. Both were divisions of the Public Health Service which, in turn, was part of the federal Department of Health and Human Services.

The Centers for Disease Control, the counterpart of the Laboratory Centre for Disease Control in Canada, is unrivalled in breadth and depth of expertise in infectious disease. During the 1980s the Centers for Disease Control played a leading role in monitoring the emergence of AIDS and in reporting it through the internationally circulated *Morbidity and Mortality Weekly Report*.

The Centers for Disease Control gave leadership and direction in the government in the prevention and control of diseases and other preventable conditions. They administered national programs for the prevention and control of communicable and vector-borne diseases, consulting as appropriate with state and local public health departments. They were responsible for disease surveillance, including the systematic collection of national data about specific diseases, the analysis and interpretation of those data, and the dissemination of the results in the United States and elsewhere. Their responsibilities included the identification and monitoring of blood-borne diseases. This task they carried out through surveillance, investigations of outbreaks of disease associated with blood or blood products, studies to assess the risk of direct and secondary transmission of specific blood-borne infectious agents, notification of appropriate government officials when known diseases or new disease-causing organisms were identified as potential threats to the safety of the blood supply, and development of preventive methods to meet new threats to the blood supply.

The National Institutes of Health was the research arm of the Department of Health and Human Services. Two of its constituent institutes had a role in protecting the blood supply. The National Institute of Allergy and Infectious Diseases conducted research on the causes and characteristics of infectious illnesses. It also studied ways to prevent, control, and treat diseases believed to be attributable to infectious agents, such as viruses, bacteria, and parasites, or to weaknesses in the responses of the body's immune system. The National Heart, Lung, and Blood Institute was involved in the development of safe and efficient methods of blood collection and distribution. Its blood division had been established in 1967 as a result of epidemiological studies that had revealed a correlation between paid blood donors and high rates of post-transfusion hepatitis, and in response to the increased demand for blood resulting from the development of advanced surgical techniques.

The World Health Organization

The World Health Organization, established in 1948 as an agency of the United Nations, had as its objective the global prevention and control of disease. Through its international networks it had become a centre for information about infectious diseases. The quality of the information the organization received varied from nation to nation. As a result, the reliability of its data about the incidence and prevalence of disease was greater for some nations than for others. The organization was also involved in investigating known and emerging diseases. To give epidemiologists a better understanding of existing and newly emerging diseases, it established four serum reference banks, located in Czechoslovakia, Japan, South Africa, and the United States, that had more than 100,000 samples in storage and had examined antibodies against various diseases from forty-five countries on five continents. The resources available to member nations, among them Canada, included international virus reference centres, a unit that investigated internationally significant diseases and developed appropriate methods of surveillance, and other units that gave assistance and advice in controlling epidemics and preventing the spread of infectious diseases. The organization's publication, *Communicable Disease Surveillance Reports*, was distributed free of charge and contained information gathered from its regional offices and reference centres and from collaborating laboratories.

In 1975, the World Health Organization and the League of Red Cross Societies organized a conference on the use and supply of blood and blood products. It recommended that nations try to become self-sufficient in blood and blood products, that donors not be compensated for giving whole blood or plasma, and that all nations enact legislation to regulate the collection, processing, distribution, export, and import of blood and blood products. These recommendations were supported at a meeting of the World Health Assembly in the same year.

The Council of Europe

The Council of Europe, an association of European nations that, in the early 1980s, had twenty-one member states, had taken an interest in the safety of blood transfusions since the late 1950s. In 1962, its public health committee established a subcommittee of experts on blood that met at least once a year and evolved into a committee of experts on blood transfusion and immunohematology. This committee had as a primary objective the establishment of common standards for a unified blood exchange system, designed to ensure that residents of member countries would receive safe blood transfusions.

The public health committee was concerned in the early 1980s about the transmission of infectious diseases through the international exchange of blood and its components and derivatives, and particularly about the transmission of diseases, including non-A, non-B hepatitis, that had long periods during which the virus was present in the blood in apparently healthy adults.

A study group issued several recommendations for blood safety. It encouraged the member countries to be as self-sufficient in blood as possible and to impose strict regulations on the eligibility of individuals to donate plasma. It urged public health authorities to collect information about the source and the use of imported plasma, and to devote additional resources to epidemiological surveillance of infectious diseases. It proposed that blood collection agencies and pharmaceutical manufacturers give treating physicians and consumers of blood products detailed information about blood and related products, including the size of the donor pool from which the products were derived, whether the donors had been paid for their blood or plasma, and the tests that had been conducted to detect the presence of transmissible diseases.

The Committee of Ministers of the Council of Europe recognized that the transmission of infections through the international transfer of blood and its components and derivatives represented a continuing health hazard for the recipients of blood and blood products. Among other matters, it was concerned about the threat posed by viral hepatitis to blood products used in treating hemophilia. It approved the following recommendation in 1981:

[T]hat national regulations be established concerning the importation of blood, its components and derivatives with a view to limiting as fully as possible potential health hazards due to the transmission of infectious agents; such regulations should, in particular, provide for the furnishing of data on the donation and the preparation of such substances, that is (in addition to the results of any specific tests which may be considered necessary by the importing state) the name of the country in which the blood was given, the date of the donation or preparation and data concerning the identity of the donor on condition that his anonymity is preserved outside the blood bank at which the donation was made; this information should be available at any time to national health administrations.

Canada was represented by an observer at meetings of the committee of experts on blood transfusion and immunohematology. From 1978 to 1991 the observer was Dr Roger Perrault, the national director of the Canadian Red Cross Society's blood transfusion service. In 1982, the Canadian government was the host at a meeting in Ottawa of the committee that was chaired by Dr Perrault and attended by Dr Denise Leclerc-Chevalier, the executive director of the Canadian Blood Committee.

The common perception of public health services in 1982

Public health activities, and the priorities assigned to them, changed greatly in the century and a quarter before the emergence of AIDS. Beginning in the last half of the nineteenth century, the most important means of saving

lives has been by improving the conditions of life. Clean water, improved sanitation and drainage, and education in hygiene and nutrition, coupled with control methods such as vaccination and quarantine, reduced the prevalence of many infectious diseases. These successes were accompanied by a growing understanding of the role of microorganisms in causing infectious disease, the methods by which diseases were transmitted, and the development of new methods of combating disease. By the early 1980s, immunization and antibiotic treatment had significantly reduced the effects of most infectious diseases, to such an extent that many persons believed they were no longer a significant problem. As one public health official testified, it was "a world where we believed, maybe very wrongly, that we had conquered infectious disease to some extent, that smallpox was eradicated and tuberculosis was no longer a problem. We had antibiotics and infections under control."

The emphasis in health care shifted during the middle of the twentieth century. Life expectancy was increasing, and the most prominent threats to life came from non-infectious ailments such as cancer, strokes, and cardiac failure. The practice of medicine became increasingly complex and costly as a result of technological advances and new procedures, diagnostic tools, and treatments. There was a greater emphasis on individual treatment and on preserving life at all costs. More of the available health care resources came to be consumed by medical care, and less was devoted to public health activities.

Public health officials also changed their focus. Infectious diseases were no longer a high priority. Special clinics existed in many communities for the treatment of sexually transmitted diseases, but even those diseases were receiving a lower priority because of the effectiveness of antibiotics. Instead, there was a greatly increased attention to the effects on health of the environment and the individual's way of life, to identifying and dealing with social conditions and individual behaviour associated with chronic disease, and to promoting good health through education in physical fitness and proper nutrition. Air, water, and soil pollution, occupational health and safety, and drug and alcohol abuse were accorded priority.

Most provincial legislation concerned with communicable diseases had changed little since the late nineteenth or early twentieth century. Under most provincial statutes, the local medical officer of health had the power to place persons infected or suspected of being infected with a communicable disease in isolation or quarantine and to require that they undergo treatment. This traditional model of infectious disease control was based on the premise that the infected persons would be contagious for a finite period and would be confined during that time, after which, if they survived, they would be released. That approach was followed for tuberculosis, typhoid, diphtheria, poliomyelitis, smallpox, and cholera. It did not take into account the danger from diseases that could be unknowingly transmitted before any symptoms developed or after the symptoms disappeared.

As the threat from infectious disease declined, so did funding for public health services and public appreciation of their value. In the early 1980s Canada was in the midst of a major recession, and provincial governments were exercising fiscal restraint. Departments and ministries of health often did not pay competitive salaries, and as a result were unable to attract expert medical and scientific professionals. Some provincial departments or ministries of health had no epidemiologist on staff in the late 1970s and early 1980s. The decentralized, regional nature of the administration of public health services, which provided a desirable flexibility in response to local needs, further hindered the ability of the provinces to undertake a coordinated and effective response to infectious disease.

8

The Care and Treatment of Hemophilia

Hemophilia is a disorder, almost exclusively found in men, that is characterized by excessive bleeding, during which the blood takes an unusually long time to clot. It is caused by an absence of one of two proteins in the patient's blood, known as the coagulation factors VIII and IX, or by a deficiency in the functioning of one of those factors. Approximately 2,500 persons suffer from hemophilia in Canada. Eighty-five per cent of them have hemophilia A (also known as classic or classical hemophilia), which is caused by a defect in the gene responsible for the production of clotting factor VIII. Hemophilia B, or Christmas disease, is caused by the lack, or diminished activity, of clotting factor IX. For the most part, hemophilia is inherited. However, approximately 30 per cent of hemophiliacs have no family history of the disease; their condition is the result of spontaneous genetic mutation. The disorder is sex linked because the genes that are responsible for the production of factor VIII and factor IX are both on the X chromosome. A normal gene can cause the production of sufficient factor to allow blood to clot normally. As a result, females, who have two X chromosomes, are rarely affected, because it is unusual for both X chromosomes to be defective. Because males have only one X chromosome, which is inherited from their mothers (along with the Y chromosome inherited from their fathers), the disorder affects males almost exclusively and, when inherited, is passed from mothers to sons.

There are also bleeding disorders caused by a deficiency of other clotting factors. The most common of these other congenital disorders, affecting both sexes, involves a deficiency of the von Willebrand factor, which is important for protecting and stimulating the production of factor VIII. A deficiency in the von Willebrand factor diminishes the amount of functional factor VIII available for the clotting process.

Hemophilia A and B are clinically indistinguishable. Both are classified as severe, moderate, or mild, depending on the level of the clotting factor present in the patient's blood. In severe hemophilia, the blood contains less than 1 per cent of the normal level of the clotting factor; in moderate hemophilia, between 2 and 5 per cent; in mild hemophilia, between 6 and 30 per cent. Two-thirds of persons with hemophilia A have it severely, and the rest are almost evenly divided between those who suffer from moderate and mild

forms of the disorder. Most persons with hemophilia B have a mild form. Although von Willebrand's disease is the most common inherited bleeding disorder, a severe form is rare.

The clinical symptoms of hemophilia are hemorrhage into joints and muscles, easy bruising, and prolonged and potentially fatal hemorrhage occurring spontaneously after trauma or surgery. Without any preventive treatment to replace the deficient clotting factors, severe hemophiliacs may experience bleeding episodes more frequently than once a week, either spontaneously or as a result of an external injury, and the bleeding may not be detected immediately. Bleeding into a joint begins with mild discomfort and a slight limitation in the movement of the joint. After several hours, the joint becomes painful and swells. Bleeding into weight-bearing joints such as the ankles, knees, and hips is more serious than bleeding into the wrists and elbows. Untreated joint hemorrhage usually leads to severe limitation in motion, permanent damage, and disabling arthritis, causing chronic pain. Bleeding into muscles is most common in the calves, thighs, buttocks, and forearms. Bleeding into the body cavity is especially dangerous because it can lead to nerve paralysis or obstruction of the airway. Bleeding into the brain and other internal organs can be fatal; until treatment with clotting factors was introduced in the 1960s, bleeding into the brain was the most common cause of death among severe hemophiliacs.

Moderate hemophilia is rarely complicated by episodes of spontaneous bleeding. However, even a minor injury may induce excessive bleeding. Mild hemophilia is associated with a normal lifestyle. If there has been no prior history of bleeding, mild hemophilia may escape diagnosis until late adolescence, and then only after significant trauma, surgery, or a dental procedure has resulted in a bleeding problem. Complications associated with hemophilia require specialized attention in otherwise routine procedures. For example, hemophiliacs may require factor replacement therapy during and immediately after a simple tooth extraction to avoid a prolonged period of bleeding.

The evolution of the treatment of hemophilia

Before modern methods of replacing the clotting factors were introduced, some of the disabling effects of severe hemophilia were reduced by techniques such as immobilizing and splinting the affected joints. Many hemophiliacs were nevertheless confined to wheelchairs because of irreparable damage to their joints. Most severe hemophiliacs could not go to school, keep jobs, or engage in rigorous physical activity because of the risk of a bleeding episode, the disabilities caused by previous hemorrhages, or chronic pain. They were often stigmatized as "sick kids" or "cripples," which led to their further isolation.

Persons with bleeding disorders require treatment with the missing clotting factor from an outside source. The objective in managing hemophilia is to raise the concentration of the deficient clotting factor to a level at which the

escape of blood is arrested, and then to maintain that level long enough for adequate healing to occur. Even a low level of clotting factor in the blood permits close to normal clotting functions. The amount of factor that must be administered depends on the level of deficiency, the patient's weight, and the magnitude of the bleeding episode. Because bleeding may recur, factor therapy is recommended even after the bleeding has stopped.

Until the 1950s, the only replacement therapy for the treatment of hemophilia involved the transfusion of whole blood. Large volumes of whole blood are needed to provide the level of factor VIII or factor IX required to control a bleeding episode, however, and the additional volume may strain the patient's circulatory system and cause heart failure.

In the 1950s, transfusions with whole blood were replaced by infusions of plasma, the liquid part of blood that contains the clotting factors. The plasma was frozen soon after the blood was donated in order to preserve factor activity, and was thawed before being used. The plasma had a higher level of clotting factor per unit of volume than whole blood; nevertheless, hemophiliacs continued to spend a great deal of time in hospital because the control of serious bleeding still required large volumes of plasma that threatened to overload the cardiovascular system. Prompt replacement therapy was the most effective means of reducing long-term damage, but the need to go to a hospital for infusions of plasma delayed treatment. Because their bleeding episodes could not be treated quickly or effectively with fresh frozen plasma, most severe hemophiliacs suffered serious musculoskeletal disabilities, endured chronic pain, and had a significantly reduced life expectancy. In the 1950s, the median life expectancy of severe classic hemophiliacs in the United States was approximately half that of all U.S. males.

Throughout the late 1950s and early 1960s, efforts were made to find a factor replacement therapy that was both effective and easy to produce and administer. In 1964 a precipitate that was rich in factor VIII that remained after fresh frozen plasma was thawed was found to be convenient to use for infusion. Cryoprecipitate, as it was called, was easy to produce. It proved much more effective than plasma in controlling bleeding in persons suffering from hemophilia A because a smaller volume was needed to deliver the same level of factor VIII. Cryoprecipitate also contained von Willebrand factor, and therefore was of use in treating von Willebrand's disease. However, cryoprecipitate does not contain factor IX, and persons with hemophilia B continued to rely on fresh frozen plasma. The Canadian Red Cross Society (Red Cross) began to produce cryoprecipitate in 1965. By the late 1960s, it was widely used in the treatment of hemophilia A in Canada. For the first time, some hemophiliacs were able to treat themselves for bleeding episodes without going to a hospital, and, with more rapid treatment, the risk of long-term damage to their health was reduced.

Cryoprecipitate made it possible to manage the majority of severe bleeding episodes without serious risk to the patient, but it was a less than perfect

therapy. For many hemophiliacs, home care remained impractical. In order to maintain the factor activity as long as possible, cryoprecipitate had to be kept in a special deep freezer at -40°C, making it difficult to store and transport, and before use it had to be thawed slowly, thereby delaying treatment. Moreover, the level of factor VIII activity in every bag of cryoprecipitate depended on the level in the plasma of the donor, which could vary considerably, depending on blood type, medications, and other individual differences among donors. As a result, it was difficult to decide how much to administer when a bleeding episode occurred. Cryoprecipitate also contained many proteins, not required in treating hemophilia, that could cause allergic reactions.

Most severe hemophiliacs, even those treating themselves at home with cryoprecipitate, still had to make many visits to hospital emergency departments. There they often experienced delays in receiving treatment because the attending physicians lacked knowledge and experience in managing a bleeding episode. It was not uncommon for a hemophiliac to diagnose a bleeding episode sooner, and with a greater understanding of how to treat it, than the physician treating him.

In 1968, the first of a new generation of more highly purified preparations containing factor VIII was licensed for use in Canada. These new anti-hemophilic factor concentrates were made by pooling the plasma from thousands of donors and extracting the factor VIII. Concentrates containing factor IX were prepared in a similar manner and first licensed in Canada in 1969. Factor concentrates were lyophilized (freeze-dried) and placed in small, easily transportable vials.

The introduction of freeze-dried concentrates transformed the management of hemophilia. Factor concentrates were more convenient than cryoprecipitate because they could be stored at home, at room temperature or in an ordinary kitchen refrigerator, for several months. They were easily prepared for treatment by adding sterile water, and could be injected in minutes. Quality control was possible because each lot was tested to determine the level of clotting factor activity.

The use of factor concentrate made home care for bleeding episodes routine. It allowed hemophiliacs to work, attend school, travel, and participate in sports and other recreational activities. It reduced the likelihood of damage to their joints and was responsible for a dramatic decrease in deaths from uncontrollable hemorrhaging. By 1980, the median life expectancy for severe hemophiliacs was near normal. The benefits were so pronounced that factor concentrate quickly gained acceptance as the product of choice for treating persons with clotting factor deficiencies. The combination of therapeutic advantage and personal convenience eventually brought about an almost universal abandonment of cryoprecipitate in favour of concentrates.

One problem persisted, however, and a new risk arose. The problem was caused by the fact that approximately 10 to 15 per cent of severe hemophiliacs develop inhibitors to the clotting factor they receive. Inhibitors are antibodies that bind to and inactivate the clotting factor, rendering replacement therapy – through the use of either cryoprecipitate or concentrate – ineffective. Mild hemophiliacs rarely develop inhibitors. A hemorrhage in a severe hemophiliac with inhibitors is difficult to control and potentially life-threatening. Until the emergence of AIDS, inhibitors were considered the most serious complication in the treatment of hemophilia. Because large quantities of factor VIII concentrate were required to overcome the inhibitors, a hemophiliac with inhibitors who experienced an extreme bleeding episode could use, in one day, as much factor concentrate as would be needed to treat a severe hemophiliac without inhibitors for a year.

Throughout the 1970s, the only way to treat hemophiliacs with inhibitors was by massive infusions of concentrate. In 1982, the Red Cross began to distribute an anti-inhibitor coagulant complex, Autoplex, that contained several other coagulant factors that could bypass the factor VIII inhibitors. Because of its high cost and the risks associated with its use, Autoplex was not made readily available. With the assistance of the Canadian Hematology Society, the medical and scientific advisory committee of the Canadian Hemophilia Society devised guidelines to govern its early distribution and to ensure that it was prescribed only when necessary.

The new risk that came with the use of factor concentrates was a result of the method of their manufacture. Thousands of units of fresh frozen plasma were pooled to produce factor VIII and factor IX concentrates. Any single unit of plasma could contain bacteria or viruses and, depending upon the micro-organism, could contaminate the entire pool and hence the final product. In contrast, every unit of cryoprecipitate was derived from the plasma of a single donor, and even though treatment normally required three to six units, the patient would be exposed to the risk associated with only a few donors rather than thousands.

The risk of transmission of hepatitis B through blood transfusion had been recognized since the end of World War II. That risk was reduced after a test to detect the hepatitis B virus in blood samples was developed; the Red Cross began using it to test all blood and plasma donations in January 1972. By the late 1970s, however, most hemophiliacs tested positive for hepatitis B antibody. By then, too, an additional risk in the use of factor concentrates – the risk of developing non-A, non-B hepatitis (most of which is now classified as hepatitis C) – was also recognized.

About half of the factor concentrate distributed in Canada was manufactured in the United States from the plasma of paid donors. Studies conducted in the 1950s, 1960s, and 1970s had demonstrated that plasma obtained from paid donors was more frequently infected with hepatitis than that obtained

from volunteer donors. Some Canadian physicians treating hemophilia were accordingly cautious in recommending the use of factor concentrates. One expressed this concern in a letter to the chair of the medical and scientific advisory committee of the Canadian Hemophilia Society in late 1979. He wrote:

I am alarmed by the fact that many patients appear to be receiving concentrate without regard to risk of hepatitis ... I think that since this [factor concentrate] is a product which definitely carries infectious risks, whose long-term implications are unknown, we should be very cautious and selective in the exposure of our patients to these risks when it is not absolutely necessary.

A study conducted in the late 1970s by Dr Agnes Bishop at a hemophilia treatment clinic in Winnipeg, and presented at a symposium sponsored by the Canadian Hemophilia Society in 1980, found that persons with hemophilia who had been treated primarily with factor concentrates had greater liver dysfunction, suggesting hepatitis, than those treated primarily with cryoprecipitate. Her findings were summarized as follows:

Dr Bishop gave figures of raised liver enzymes in 50% of patients treated with concentrates against 15% of patients treated with cryoprecipitate. However, she points out that cryoprecipitate has been in use very much longer than concentrate and, therefore, the figures appear much worse for the concentrate product.

Dr Andrew Kaegi, the medical director of the Red Cross blood transfusion centre in Calgary from 1977 to 1981, found Dr Bishop's results frightening. He was one of the physicians who resisted pressures to switch hemophiliacs from cryoprecipitate to factor concentrates. Dr Thomas Bowen, who succeeded Dr Kaegi in 1981, also believed that cryoprecipitate was safer than lyophilized factor concentrates because it was produced locally from the plasma of Canadian volunteer donors. As a result of physicians' concerns and educational programs conducted by concerned hemophiliacs, the use of cryoprecipitate almost doubled in Calgary in 1982. The use of cryoprecipitate also increased significantly in Regina, London, Hamilton, Ottawa, Quebec City, and Saint John, in 1983 and 1984. Later studies found that the rate of infection with HIV among hemophiliacs was lower in Calgary than elsewhere in Canada.

Despite the recognized risks, most Canadian physicians treating hemophiliacs favoured the use of factor concentrates over cryoprecipitate. Some hemophiliacs suffered liver failure and death from hepatitis, but the incidence of these occurrences was relatively low before the 1970s. It was reported at the symposium sponsored by the Canadian Hemophilia Society in 1980 that a "[s]urvey of the causes of death of hemophiliacs in the 1950's and 1960's does

not feature severe liver disease as a cause." Surveys conducted in the late 1970s demonstrated that a "high percentage" of hemophiliac patients had raised liver enzymes, and liver biopsies performed at some treatment centres showed patterns of chronic hepatitis. However, it was considered "uncertain whether these changes would lead to any morbidity or premature mortality." Physicians treating hemophiliacs and the Canadian Hemophilia Society believed that the benefits associated with factor concentrates far outweighed the risk of contracting hepatitis, especially since most adult hemophiliacs had already been exposed to hepatitis B. Although non-A, non-B hepatitis was recognized, its seriousness was not yet appreciated.

By 1980, factor concentrates were frequently being used prophylactically. The principle of prophylaxis – or maintenance therapy, as it was sometimes called – was that regular infusions of factor concentrate would raise the level of the patient's clotting factors to a point that would decrease the risk of spontaneous hemorrhage. The prophylactic use of factor replacement therapy had been recommended as early as 1958 in Sweden and by the mid-1970s in Canada. For a small minority of hemophiliacs, for whom the risk of a life-threatening cerebral hemorrhage increased every year, prophylactic treatment was considered essential. Any increased use of factor concentrates, however, correspondingly increased the risk of exposure to infected donations.

Many hemophiliacs placed themselves on a prophylactic program. Although the use of factor concentrates for emergency treatments for most of these patients might have declined, their annual consumption of concentrates often increased. For example, in the province of Quebec, where many hemophiliacs were on active prophylactic programs, hemophiliacs used more concentrates, on average, than hemophiliacs in the rest of Canada. The number of units of replacement factor distributed by the Red Cross increased each year between 1978 and 1982 more rapidly than the comparable increase in the Canadian population. The demand was increasingly met with concentrates. The use of cryoprecipitate declined dramatically from 1978 to 1980, when it levelled off for several years. There were, however, few national or international guidelines for determining therapeutically appropriate levels of use of factor concentrates. The average annual consumption of factor VIII per patient in home care ranged, internationally, from 8,000 units in Japan to approximately 100,000 units in Germany. This broad range, found in a survey of eleven countries, was said to "reflect availability as much as anything else." Consumption also varied widely in Canada. Among severe hemophiliacs who used factor concentrates, the amounts ranged between 10,000 and 100,000 units a year. In the event of surgery or acute traumatic hemorrhage, more than 250,000 units could be required.

In 1982, the Red Cross distributed a total of 53 million units of anti-hemophilic factor. This was the equivalent of approximately 40,000 units of factor VIII for each person with hemophilia A. The annual average use per patient, including surgical procedures, varied among individual centres,

from 18,250 units in Regina to 63,200 in Montreal. Four-fifths of the amount distributed nationally in 1982 was in the form of concentrates, and the remainder in cryoprecipitate. However, the proportion varied from centre to centre. In Calgary, for example, the distribution of factor VIII was almost equally divided between factor concentrates and cryoprecipitate; in several other centres, cryoprecipitate made up less than 10 per cent of the total consumption.

The role of the Canadian Red Cross Society

In the early 1970s, when factor concentrates were first available in Canada, hospitals bought them from their own budgets, and some hemophiliacs obtained them with a physician's prescription, at their own cost unless the cost was included in their province's health insurance plan. Although health costs were shared by the federal and the provincial governments, each province determined whether its health insurance should be extended to include factor concentrates.

In 1978, the Red Cross proposed a change intended to achieve economies of scale and to ensure a more equitable distribution of factor concentrates throughout the country. It suggested that the ministers of health authorize the additional funding that would permit it to become the sole purchaser and distributor of factor VIII concentrate in Canada. The Red Cross had been distributing the much smaller quantities of factor IX concentrate required nationally since 1976. It said that a single point of distribution for all factor concentrates would, in addition to other benefits, facilitate the collection of demographic and therapy-related data about hemophiliacs, and thereby enable it to project more reliable estimates of future needs. The Red Cross asked the medical and scientific advisory committee of the Canadian Hemophilia Society to determine the conditions under which factor concentrates should be used, to help it estimate requirements.

Canadian hemophiliacs respected the Red Cross for its expertise in blood products and transfusion practice. It had long served as the lifeline for Canadian hemophiliacs. Several hemophiliacs acted as spokespersons for Red Cross blood donor campaigns, and photographs of hemophiliacs frequently appeared on campaign posters. Hemophiliacs saw the Red Cross, with its national blood program, established relationship with manufacturers, and reliance on volunteer donations, as the organization best able to provide the safest blood products on the most equitable basis. The Canadian Hemophilia Society and the Canadian Hematology Society were instrumental in persuading the federal and the provincial ministries of health to fund a centralized program of purchasing factor VIII concentrate. A description of the national program appeared in the newsletter of the Red Cross's Toronto blood centre in December 1978:

There will be no direct charge made to the hospital for ... lyophilized [freeze-dried] Factor VIII [concentrate]. The cost for the contract purchase of commercial concentrate is covered by combined Provincial and Federal

government funds. There should be no further need for individual hospitals to purchase Factor VIII [concentrate] from the various pharmaceutical companies.

The Red Cross proposed distributing factor concentrates to each province according to the information available about the number of hemophiliacs in the province and the province's previous purchases. In order to create accurate records of the number of hemophiliacs in Canada and their needs for treatment, the Canadian Hemophilia Society had conducted a nationwide survey in 1977 to determine the number of Canadians with hemophilia, classified by type and by severity. That information constituted the first national registry of hemophiliacs. It was used by the Red Cross to estimate its blood centres' requirements for factor concentrates and to estimate total future demand. The registry was out of date by 1982; in that year the Canadian Hemophilia Society identified the establishment of an accurate database as one of its priorities.

In December 1978, the Red Cross sent its blood centres the first shipments of factor VIII concentrate manufactured as part of the national program. At first, shipments of factor VIII concentrate were made every six weeks, with each centre's allocation based on the expected requirements in its area. The Red Cross urged the medical directors of the blood centres to try to ensure that the distribution was equitable and fair. Some difficulties were encountered in the program, however; one blood centre had not received any factor concentrate by May 1979.

The role of the Red Cross and its medical directors was to supply, through its seventeen blood centres, the blood components and products requested by local hospitals and treating physicians. The medical directors were reluctant to advise hemophiliacs about appropriate treatment directly, but they were often consulted by physicians. In addition, the *Clinical Guide to Transfusion*, first published by the Red Cross in 1980 and revised from time to time, was an important reference work that was distributed to all hospitals.

The Red Cross distributed several brands of factor VIII and factor IX concentrates in Canada. More than half the factor VIII concentrate was produced from plasma collected from paid donors in the United States. The other concentrates were produced from plasma collected from volunteer donors in Canada. Because the factor concentrates were part of the national program and were supplied at no cost to the user after 1978, little, if any, consideration was given to alternative products or sources of supply.

The Canadian Hemophilia Society

In August 1953, a small group of hemophiliacs and their families met in Montreal to discuss the formation of a Canadian chapter of the U.S. National Hemophilia Foundation to act as a support group to hemophiliacs and their

families. The Canadian Hemophilia Society was established a few months later, independently of its U.S. counterpart, to meet Canadian needs more appropriately. Between 1953 and 1968, local chapters were formed in every province. The society became a national service and advocacy organization on behalf of all persons with bleeding disorders.

The Canadian Hemophilia Society was incorporated in 1977 as a voluntary lay organization with the purpose of assisting hemophiliacs "in every way possible." Its objects included (a) encouraging and assisting in the treatment and medical care of sufferers; (b) encouraging and promoting research in hemophilia; (c) aiding in the education of parents and the general public in the problems of hemophilia; (d) using its best efforts towards the procurement of supplies of whole blood, blood plasma, or other therapeutic materials that help in the clotting of blood; (e) establishing facilities for the adequate treatment of all aspects of hemophilia; and (f) soliciting, collecting, or otherwise raising money for purposes directly applicable to the treatment of hemophilia and the assistance of hemophiliacs.

In 1982, as today, membership in the society was open to all family members and friends of hemophiliacs free of charge. The society was governed by an executive committee and board of directors, the members of which, except for the society's executive director, were volunteers. The directors were hemophiliacs or family members of hemophiliacs, and every province was represented. The society held annual general meetings and educational seminars. It was financially supported through government grants and donations from organizations, foundations, and individuals. Donations from pharmaceutical companies were designated for specific projects such as the society's quarterly publication, *Hemophilia Today*.

The Canadian Hemophilia Society was the only national lay organization directly involved in the Canadian blood system. Although it had no formal role in that system, a member of the society sat on the advisory subcommittee of the Canadian Blood Committee. That committee, established in 1981, funded and established policy for the Canadian blood system.

The Canadian Hemophilia Society was one of the founding members of the World Federation of Hemophilia. It had no formal connection with the U.S. National Hemophilia Foundation, but members of the executives of the two organizations communicated informally, and some members of the Canadian Hemophilia Society regularly attended meetings of the National Hemophilia Foundation.

The society's quarterly newsletter was an important source of information about advances in the treatment of their disorder and any attendant risks. The newsletter was mailed to every person on the society's list. Approximately one-third of the hemophiliacs identified by the national survey in 1977 had been previously unknown to the society, however, and had not received its educational materials.

The Canadian Hemophilia Society had advisory committees. One was a blood resources committee, consisting mainly of lay persons, that addressed issues of safety and the adequacy of blood products used by hemophiliacs. Another was a medical and scientific advisory committee that was composed for the most part of treating physicians and other health care workers involved in the management of hemophilia.

The medical and scientific advisory committee was primarily responsible for giving expert "counsel and assistance to the [society] and guidance to other concerned bodies on medical, scientific and professional matters pertaining to the care of hemophiliacs." The committee's duties included the drafting of recommendations for the comprehensive management of hemophilia; it was also expected to cooperate with the society, the Red Cross, and governmental and private agencies in addressing issues of importance to the welfare of hemophiliacs.

The members of the medical and scientific advisory committee were appointed by the board. They served voluntarily and met at least once a year, usually in conjunction with the society's annual general meeting. The chair of the committee was a member of the board of directors of the society. The committee had no offices, no support staff, and no budget of its own. It was composed of medical and allied professionals involved in the care of hemophiliacs, including dental consultants, physiotherapists, nurses, and social workers.

Provincial or local chapters of the Canadian Hemophilia Society had their own medical and scientific advisory committees. The chairs of the provincial committees, all of whom were physicians, sat on the national medical and scientific advisory committee so that they could share information and work towards consistent quality of treatment for hemophiliacs nationally. Practitioners in several health care fields, including nursing, physiotherapy, social services, orthopedics, and dentistry, were appointed to the committee by its chair. The provincial committees acted as the liaison between the local chapters and the hemophilia-treating physicians. Some of the physicians on these committees were medical directors or assistant medical directors of their local Red Cross blood centres.

The medical and scientific advisory committee was not represented on any of the advisory committees of the Red Cross. Beginning in 1980, the committee recommended to the Red Cross that a coagulation product working group be created that would include physicians who were treating hemophiliacs, giving them an opportunity to participate in the decisions about the products that would be purchased and distributed. No such committee was established. However, in September 1983, the director of blood product services of the Red Cross blood transfusion service, Dr Derek Naylor, joined the society's medical and scientific advisory committee as a consultant.

The medical and scientific advisory committee assumed the responsibility for drafting guidelines for the distribution of plasma-derived products and other drugs used in the treatment of hemophilia when they were in short supply. This allocation happened, for example, when limited supplies of factor VIII concentrate were first distributed to hemophiliacs as part of the national program in early 1979. The Red Cross had made it clear that it wanted no involvement in the allocation of the product "beyond assuring ... that the available supply will be fairly and equitably distributed throughout the nation." The committee created a list of recommended priorities for the distribution of factor VIII concentrate that was applied during that period of short supply. It also created the guidelines for the distribution of Autoplex when that product was introduced in 1982.

The development of comprehensive-care clinics

Because hemophilia is a chronic disorder with many and varied complications, its appropriate care involves a number of specialties. In the 1970s, the care of hemophiliacs in Canada was fragmented. Health care was delivered through hospitals and individual physicians, including hematologists, pediatricians, internists, and family physicians, with little coordination among them. Hemophiliacs tended to cluster around the hospitals in which their physicians practised. Because those hospitals dispensed or administered coagulant blood products, they came to be associated with the care of hemophiliacs. However, they did not adequately meet the complex range of special needs for the treatment of hemophilia.

Because of the fragmented nature of the care, its quality was inconsistent. The national survey of hemophiliacs conducted in 1977 found that, of the 1,009 hemophilia A patients identified, 688 were using cryoprecipitate, ninety were using factor concentrates, sixteen were using fresh frozen plasma, four were using whole blood (which was by then considered unacceptable therapy), and fifty-two were receiving "a wide variety of different preparations." The other 159 were not receiving any blood or blood product therapy.

Because of the small number of Canadians who suffered from hemophilia and their wide geographic distribution, very few physicians specialized in their care. According to the 1977 national survey, the physicians treating hemophiliacs were most often hematologists. However, one in five hemophiliacs received factor replacements under the supervision of a family physician, and the Canadian Hemophilia Society's medical and scientific advisory committee was concerned that many of those physicians did not have the expertise required for the routine care of hemophiliacs. In particular, non-specialists lacked the experience that would enable them to respond quickly to complications. Non-specialist care was especially common in rural areas. These concerns caused the medical and scientific advisory committee of the Ontario chapter of the Canadian Hemophilia Society to issue guidelines in 1979, directed to the staff members of hospital emergency rooms, for the care of hemophilia.

During the 1970s, hemophiliacs, their families, their treating physicians, and the Canadian Hemophilia Society began to lobby for the establishment of comprehensive-care clinics. Comprehensive treatment centres for hemophiliacs had been established in the United States during the 1960s and had been shown to improve the health of hemophiliacs and to reduce the length of time they spent in hospital. The comprehensive approach encouraged the development of expertise among the hematologists, rheumatologists, orthopedic surgeons, dentists, nurses, social workers, psychiatrists, psychologists, and physiotherapists involved in the care of hemophilia. By making these services available in one place and providing for the multidisciplinary management of hemophilia there, the comprehensive-care centres were able to meet the broad range of needs and complications associated with the disorder more effectively.

The lobbying efforts succeeded. British Columbia opened its first comprehensive-care clinic in 1973; Ontario, in 1975; Quebec, in 1976; Alberta, in 1977; and Newfoundland, in 1978. By 1982, most provinces had at least one comprehensive-care centre, and 75 per cent of hemophiliacs had a comprehensive-care centre available to them.

The comprehensive-care centres were funded by the provincial ministries of health, and most were established as part of a university teaching hospital. Each had a director who was a treating physician, and a nurse coordinator who served as the primary contact with hemophiliacs and their family members and arranged for the services, when required, of the other members of the multidisciplinary team. The comprehensive-care centres provided routine and emergency care. They conducted training programs in self-infusion to encourage patients to treat bleeding episodes promptly at home. They made regular appointments for patients in order to monitor the patients' health and use of blood products.

The introduction of comprehensive-care clinics did not eliminate entirely the problems associated with the management of hemophilia. Some hemophiliacs attended the clinics for assessment less frequently than was recommended – that is, every twelve months for persons with moderate or mild hemophilia, and every six months for severe hemophiliacs. For hemophiliacs who lived in remote parts of the country, comprehensive treatment centres were practically inaccessible. Receipt of factor concentrates was not dependent upon registration or attendance at a clinic, except in the province of Quebec, where hemophiliacs had to register at one of four clinics to obtain blood products. Elsewhere a hemophiliac could obtain a prescription for a coagulant blood product from any physician. Because comprehensive-care centres were not the only organizations distributing blood products to hemophiliacs except in Quebec, it was difficult to track the use of blood products, advise all patients adequately about their care, and recall contaminated products effectively.

The system of comprehensive care for hemophilia in Canada has remained fundamentally unchanged since the mid-1980s. Approximately 2,000 persons with hemophilia receive their medical care at one of more than twenty comprehensive-care programs throughout the country. Quebec remains the only province requiring hemophiliacs to register at a clinic to receive treatment. Clinics in the other provinces rely on voluntary registration. The Association of Hemophilia Clinic Directors of Canada, a professional association composed of specialist physicians who treat hemophilia patients in comprehensive-care facilities, is in the process of creating a computer-linked, national registry for hemophiliacs. It is intended to allow closer monitoring of the use of blood products and their efficient retrieval if necessary.

The extent of home care

The development of factor concentrates made it possible for hemophiliacs to treat themselves at home and to have a high level of independence. It also made it increasingly difficult for their physicians to monitor their treatment and progress and to detect complications. Hemophiliacs treating themselves at home were supposed to record their use of concentrates so that their physicians could assess the efficacy and safety of the therapy, but not all did so regularly. Some hemophiliacs obtained their concentrates through renewable prescriptions and had little or no systematic medical supervision. Some comprehensive-care centres encouraged accurate recording by insisting that their patients bring their empty vials and their "bleed sheets" to the centre before a new supply of concentrate was issued, but no centre denied a hemophiliac treatment. Physicians treating hemophiliacs believed that a comprehensive-care clinic could manage the disorder more effectively than an individual physician, but in 1977, according to the national survey, only half the severely affected hemophiliacs were receiving any form of regular assessment at a hemophilia clinic.

By the spring of 1982 it was clear that many Canadian hemophiliacs welcomed the opportunity to manage their own care at home. Some of these patients received little or no supervision from their clinics or prescribing physicians, and, as a result, some of them did not regularly obtain current medical information or professional advice about the risks associated with their treatment. A number of hemophiliacs, especially those suffering from mild hemophilia, had never been assessed by a treating physician, and many hemophiliacs, including some suffering from severe hemophilia, did not appear on the national hemophilia registry or the Canadian Hemophilia Society's mailing list. The convenience of factor concentrates in treating bleeding episodes, and the prophylactic protection and revolutionary improvement in life-style they afforded, led many hemophiliacs to view the risk of hepatitis associated with the use of factor concentrates as an acceptable

risk. Very few Canadian hemophiliacs recognized in late 1982 that the risk of infections associated with the use of factor replacement therapy, and of freeze-dried factor concentrates in particular, extended to AIDS.

The risks attendant upon the use of factor concentrates have been reduced in the years since the emergence of AIDS. Virally inactivated factor concentrates were introduced in 1985. In the late 1980s, more highly purified factor concentrates became available, and in 1992 a factor VIII preparation made by recombinant DNA technology was licensed by the Bureau of Biologics. Because recombinant factor VIII preparations are not derived from human plasma and do not carry the risk of transmitting infectious disease agents from humans, most persons with type A hemophilia started using recombinant factor VIII in 1993. Through the early to mid-1990s, most persons with hemophilia B used a highly purified, plasma-derived factor IX concentrate that had not been licensed by the bureau and could be obtained only through the emergency drug release program. A recombinant factor IX preparation was licensed by the bureau in 1997.

PART III

The Canadian Response to Threats to the Safety of the Blood Supply

9

The Recognition of AIDS as a Blood-Borne Disease

This brief description of the emergence of AIDS and of the development of knowledge that the disease was blood borne relies almost exclusively on events and articles published in the United States. AIDS was, of course, prevalent in other parts of the world, particularly in Africa, but the focus on the United States is a reflection of the fact that events in the United States served to inform Canadians about the disease and had a significant influence on our response to the emergence of AIDS.

In late 1980 and early 1981, the Centers for Disease Control (CDC) in Atlanta, Georgia, a division of the Department of Health and Human Services, began to receive reports of male homosexuals suffering from Kaposi's sarcoma, a rare form of skin cancer that until then had been seen only in elderly men, and from *Pneumocystis carinii* pneumonia, which until then had been found only in patients with severely weakened immune systems. During this period, a marked increase was seen in requests for pentamidine, a drug used in the treatment of *Pneumocystis carinii* pneumonia that could be obtained only from the CDC. On 5 June 1981, the CDC's *Morbidity and Mortality Weekly Report* included a report of five cases of *Pneumocystis carinii* pneumonia that were strikingly similar. All five patients were homosexual men who had used inhalant drugs and had cytomegalovirus infection and candidiasis. Cytomegalovirus and candida are microorganisms commonly found in humans. They cause opportunistic infections in persons with weakened immune systems but do not usually cause disease in other persons. Four of the patients showed evidence of past hepatitis B infection and three had abnormal cellular immune function. These findings were said to suggest "the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections." A month later, the CDC reported that twenty-six cases of Kaposi's sarcoma and ten more cases of *Pneumocystis carinii* pneumonia had been diagnosed among homosexual men in New York City and California during the previous thirty months. In August 1981 it reported seventy more cases of Kaposi's sarcoma or *Pneumocystis carinii* pneumonia, the vast majority among homosexual or bisexual men. In that report, the clustering of both diseases among homosexual men was seen to suggest a common underlying factor. The article

went on to say that “[b]oth diseases have been associated with host immunosuppression, and studies in progress are showing immunosuppression in some of these cases. The extent or cause of immune suppression is not known.” The new disease was provisionally named Gay Related Immunodeficiency Disease, or GRID.

By the end of 1981, the CDC was investigating 160 cases of GRID, and five to six new cases were being diagnosed every week. The authors of an article published in the *New England Journal of Medicine* of December 1981 warned that a “nation-wide epidemic of immunodeficiency among male homosexuals” was taking place. There was also evidence that the epidemic was beginning to affect new risk groups. Intravenous drug users were now also suffering from these opportunistic infections. Another study published in the *New England Journal of Medicine* in December 1981 found that of eleven new cases of *Pneumocystis carinii* pneumonia, six were homosexual men and seven were drug users. Of the seven who were drug users, five had a recent history of intravenous drug use.

The mortality rate associated with GRID – then recorded at almost 40 per cent – was cause enough for concern, but the association of the new syndrome with male homosexuals was particularly troubling to epidemiologists. Dr Donald Francis, then the assistant director for medical science in the CDC’s division of virology, testified that

gay men had been known to be a bellwether of new epidemics to come, be they syphilis or gonorrhea or gastrointestinal diseases or hepatitis. Once diseases got into the gay community they spread very, very effectively, usually from coastal cities into the interior of the United States and then out. So the occurrence of any new disease in the gay population was something that we all considered something to watch very carefully.

Moreover, during the early 1980s, gay men were frequent blood donors. The results of studies on the prevalence of male homosexuality vary widely. Although some studies suggest that 2 per cent of adult men are homosexual, other studies suggest that the prevalence may be as high as 10 per cent.

To ensure that new cases of opportunistic infections were properly monitored and investigated, in July 1981 the CDC created an internal task force led by Dr James Curran, the chief of its venereal disease control division, to study Kaposi’s sarcoma and opportunistic infections. The task force undertook passive surveillance (obtaining data from telephone reports, from requests for pentamidine, and from reports from state health departments, physicians, and gay community networks); active surveillance in eighteen major cities (communicating with the heads of the infectious disease, dermatology, oncology, and pathology departments of all major hospitals); interviews with patients to identify the syndrome’s characteristics and factors; and a national case control study to search for clues to the cause of the disease.

By March 1982, 257 cases had been reported. Of these, 102 persons had Kaposi's sarcoma alone, 112 had *Pneumocystis carinii* pneumonia alone, and twenty-five had both. In the eighteen other reported cases, other opportunistic infections had been identified in previously healthy persons. Investigators identified two distinctive clinical features. First, the patients appeared to be suffering from immunosuppression. CDC officials thus concluded that the outbreak of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia "appear[ed] to be based upon a severe defect of the immune system," demonstrated by a reversal of the T-helper/suppressor ratio. Second, the patients appeared to have suffered, several months to years before the onset of the disease, from a condition characterized by fever, weight loss, malaise, and persistent swollen lymph glands (lymphadenopathy).

In January 1982, a report of the CDC task force reproduced in the *New England Journal of Medicine* stated:

[i]f immunosuppression is the underlying cause of these conditions, then Kaposi's sarcoma and *Pneumocystis carinii* pneumonia may represent the "tip of the iceberg," including other conditions that are less readily recognized or have longer latency periods. While investigating this outbreak, we have received numerous physicians' reports on young homosexual men with nonfatal opportunistic infections, unexplained prolonged lymphadenopathy, or lymphoreticular neo-plasias [cancer of cells associated with the immune system].

If the "iceberg hypothesis" were true, the patients already diagnosed with Kaposi's sarcoma and *Pneumocystis carinii* pneumonia were only the part of the iceberg above the water. Those with persistent lymphadenopathy might go on to develop the same or other fatal opportunistic infections. That group would be the much larger underwater part of the iceberg. The possibility was a major concern for public health officials.

In March 1982, the CDC convened its first interagency meeting in an effort to recruit the assistance of the Food and Drug Administration and the National Institutes of Health in laboratory research and in investigating the history and cause of the disease; the administration and the institutes were the other divisions of the Public Health Service, a branch of the federal Department of Health and Human Services. By this time, several different hypotheses had been advanced to explain the cause of the immune suppression. One was that it resulted from exposure to cytomegalovirus; a second, that it was caused by use of amyl nitrite, or "poppers," a street drug that was popular at that time, especially among gay men; a third, that the immune system was impaired by repeated exposure to foreign substances; and a fourth, that the disease was caused by a new infectious agent. There was evidence to support all these hypotheses, but by the end of 1982 all but the last had effectively been discarded.

The association with cytomegalovirus was made early in the epidemic. Evidence of previous or existing infection with it was common in reports of cases of GRID involving Kaposi's sarcoma and *Pneumocystis carinii* pneumonia. It had already been well established that cytomegalovirus could cause immunosuppression and that there was a high incidence of the infection among homosexual men. It was therefore suggested that the immunosuppression and resulting infections were caused by reinfection with cytomegalovirus from exposure to the semen or urine of sexual partners. That hypothesis, however, failed to account for the fact that homosexuals with cytomegalovirus had only recently begun to suffer from opportunistic infections. By December 1981, experts were suggesting that GRID might be caused by a new, more virulent strain of cytomegalovirus. In April 1982, however, a previously healthy homosexual man with no history of either cytomegalovirus or Kaposi's sarcoma was reported to have died from *Pneumocystis carinii* pneumonia. Further evidence accumulated that cytomegalovirus was not the cause of the syndrome. By late 1982, although it was acknowledged that cytomegalovirus could not be ruled out entirely, it was widely believed that it was almost certainly not the primary cause of the immunosuppression.

The link with amyl nitrite was, on the surface, at first impressive. Amyl nitrite was the only apparently new risk factor. A study of 300 homosexual men by the CDC found that 88 per cent had used the drug within the previous five years, and another study found an association between exposure to amyl nitrite, sexual promiscuity, and the development of Kaposi's sarcoma. Furthermore, there was evidence that nitrites caused tumours in the lymph systems of laboratory rats. During 1981 and 1982, researchers explored the possibility that a drug or toxin such as amyl nitrite could increase the susceptibility of persons to infection with opportunistic organisms, or that nitrites could in some way distort the host-parasite relationship of cytomegalovirus. Research published in the second half of 1982 undermined that hypothesis, however. One study, published in the *British Medical Journal* of 3 July 1982, found no consistent use of nitrites among those suffering from the new syndrome; another found no correlation between the use of amyl nitrite and altered T-cell levels among homosexual men.

Closely allied with the amyl nitrite hypothesis was the suggestion that repeated exposure to foreign substances, or antigens, found in semen and street drugs might overload the immune system and cause it to break down. This would account for the fact that homosexual men and intravenous drug users were at risk of contracting the disease. The hypothesis was later extended to explain the emergence of opportunistic infections among those hemophiliacs routinely treated with factor concentrates, blood products prepared from the pooled plasma of many thousands of donors. (Factor concentrates contain antigens, which the body recognizes as foreign.) This hypothesis did not explain, however, why the disease was prevalent among homosexual men and intravenous drug users living in several large urban centres but not among

those living in smaller communities throughout the United States. Nor did it explain why hemophiliacs who had for years been treated with cryoprecipitate, a blood-clotting product prepared from the plasma of a small number of donors, were only now beginning to suffer from immune deficiencies. An article in *Science* in August 1982 pointed out that "[t]he hypothesis ... suffers from the problem of failing to explain how a new disease might have arisen."

The suggestion that the disease might be caused by an infectious agent arose in late 1981, and by the spring of 1982 it was considered a strong possibility. At the interagency meeting in March 1982, the CDC investigators reported that "[s]ome microorganisms are known to produce transient immunosuppression, but it is typically neither profound nor irreversible, suggesting that if the cause of the epidemic is an infectious agent, it is a new one." Supporting evidence appeared in June 1982, when the CDC identified a cluster of nineteen homosexual men in California who had Kaposi's sarcoma, *Pneumocystis carinii* pneumonia, or both. Since several of these patients had had sexual contact with one another, the CDC concluded that "[i]nfectious agents not yet identified may cause the acquired cellular immunodeficiency that appears to underlie KS [Kaposi's sarcoma] and/or *Pneumocystis carinii* pneumonia among homosexual males," and that sexual partners of patients might be at increased risk. The patients developed symptoms between nine and twenty-two months after sexual contact, indicating a relatively long incubation period. From the data, it also appeared that during the incubation period persons were infectious although no symptoms were evident.

Among the four hypotheses, the emergence of a new infectious agent best explained why the disease had recently appeared among both intravenous drug users and homosexual men. Both groups are exposed to the blood or bodily fluids of other persons. The hypothesis became all the more convincing as the disease came to be reported among new risk groups.

In June 1982, the CDC formulated the first definition of what came to be known as AIDS. The CDC's definition, which was adopted in other countries, was modified over time to reflect the current knowledge about AIDS. In its first form, the definition was:

illness in a person who 1) has either biopsy-proven KS [Kaposi's sarcoma] or biopsy- or culture-proven life-threatening opportunistic infection, 2) is under the age of 60, and 3) has no history of either immunosuppressive underlying illness or immunosuppressive therapy.

This first definition focused on the final stage of the disease, and not on the first signs and symptoms of AIDS or its precursor states. A "case" of AIDS was one that could be verified by CDC officials as falling within this strict definition; frequently, the number of such cases exceeded those reported in the *Morbidity and Mortality Weekly Report* because of the delays inherent in investigation and publication.

In June 1982, the CDC reported that the incidence of AIDS had risen significantly within the heterosexual population. Of the 355 cases reported, 16 per cent were heterosexual (three-quarters men, one-quarter women), and only about half of these persons were intravenous drug users. A study of heterosexual patients was in progress to determine whether the progression of the disease and the patients' medical histories, sexual practices, or use of drugs were in any way similar to those of homosexual patients.

By July 1982, the CDC had also received thirty-four reports of cases of opportunistic infections among Haitians who had recently arrived in the United States. The patients were heterosexual men and women who had no history of intravenous drug use. The CDC recognized these cases as a "new phenomenon," but was uncertain whether they were related to similar outbreaks among homosexual men and intravenous drug users. (Eventually it was shown that heterosexual Haitian men were likely to have been exposed to the disease during homosexual encounters with men visiting Haiti from New York.) During the same month, the CDC began to receive reports of the disease among prison inmates and persons with hemophilia.

By the summer of 1982, there was substantial evidence that the disease was caused by an infectious agent transmissible by blood. Two groups had been identified who were apparently at risk – not from sexual contact, but from the sharing of blood. These were intravenous drug users who shared needles (and thereby were exposed to the blood of other users), and hemophiliacs who used factor concentrates.

In late June 1982, Dr Curran reported to the task force on Kaposi's sarcoma and opportunistic infections that the CDC was investigating reports of *Pneumocystis carinii* pneumonia among hemophilia patients. Three cases had been identified, one in Florida, one in Colorado, and one in Ohio – sites that were scattered and distant from the centres in which the disease had until then been concentrated (that is, New York, San Francisco, and Los Angeles). Dr Bruce Evatt, a member of the task force, then wrote to Dr Louis M. Aledort, a medical adviser to the National Hemophilia Foundation, that "we have been quite concerned about the possibility that the causal agent is a virus" and that, because the disease appeared to be transmitted in a manner similar to that in which hepatitis is transmitted, hemophiliacs "would be prime candidates to develop this syndrome."

Upon learning of this threat to hemophiliacs, the CDC decided without delay to convene a small ad hoc expert advisory committee, composed of representatives from the CDC, the Food and Drug Administration, the National Institutes of Health, and the private sector to identify the implications of this latest report for blood products and to make recommendations within thirty days to the assistant secretary for health. On 9 July, the director of the CDC, Dr William Foege, reported the three cases to state and territorial health officers, blood-banking organizations, the Food and Drug Administration, the National Institutes of Health, and regional offices of the CDC. He told

them that the reported immune dysfunction among the three hemophiliacs might be caused by a transmissible agent and that "concern about possible transmission through blood products has been raised." He said the CDC would be conducting surveillance, and asked hemophilia treatment centres to report cases of opportunistic infections or suspected immune deficiency to the CDC immediately through state health departments.

On 14 July the National Hemophilia Foundation informed hemophilia patients and treating physicians about the three cases. It said that the CDC believed that the immune deficiency might be caused by a virus transmitted through blood or blood products as was hepatitis, but that the risk of contracting this immunosuppressive agent was minimal.

A report of the three cases of *Pneumocystis carinii* pneumonia in hemophiliacs appeared in the *Morbidity and Mortality Weekly Report* of 16 July 1982. The investigators concluded that, since the patients lived in different states and had not received common lots of factor concentrate, "[a]lthough the cause of the severe immune suppression is unknown, the occurrence among the three hemophiliac cases suggests the possible transmission of an agent through blood products." On the same day, officials of the Office of Biologics, the federal agency regulating the U.S. blood and blood products industry, met with representatives of the CDC, the National Institutes of Health, the National Hemophilia Foundation, and various blood-banking organizations to determine whether any common factor could be identified among the three cases reported among hemophiliacs and the earlier cases known among homosexuals and drug users. At this meeting, a committee on opportunistic infections in patients with hemophilia was established to exchange information about the cases and to conduct surveillance.

That committee met in Washington, DC, on 27 July 1982. It was attended by representatives of the key federal agencies (the CDC, the Food and Drug Administration, and the National Institutes of Health), a number of national organizations involved in the blood system (the American Association of Blood Banks, the American Red Cross, the American Blood Resources Association, the Council of Community Blood Centers), the National Hemophilia Foundation, the Pharmaceutical Manufacturers Association, and the National Gay Task Force (the largest gay civil rights organization in the United States). The meeting had two issues before it. They were whether the cause of immunodeficiency in hemophiliacs was the same as the cause of immunodeficiency in members of other high-risk groups, and whether certain blood products placed recipients at risk of contracting this form of immunodeficiency.

There was agreement that the disease was caused by an infectious agent and that those at risk of developing the disease included intravenous drug users and Haitians, in addition to homosexual men. The task force accordingly decided that the disease should be renamed the "Acquired Immune Deficiency Syndrome," or AIDS. It considered the occurrence of *Pneumocystis carinii*

pneumonia in hemophiliacs "disturbing" because that disease was not common among hemophiliacs and because two of the three hemophiliac patients reported as having it also had T-cell abnormalities similar to those in patients in other groups at high risk of developing AIDS. Whether hemophiliacs were at risk of contracting AIDS from blood products was not yet considered clear, but it was agreed that the possibility must be explored. The meeting therefore recommended that a surveillance study of hemophiliacs be carried out, that laboratory studies be undertaken of hemophiliacs with no symptoms of opportunistic infections, and that techniques be developed immediately to reduce or eliminate the risk of infection from factor VIII concentrate. On 30 July, the National Hemophilia Foundation announced that its national office would work directly with the CDC, the Food and Drug Administration, and the National Institutes of Health to establish a surveillance program of its members to determine whether any patterns of AIDS transmission could be recognized among persons with hemophilia. That study began in late October and early November in collaboration with the CDC.

In September 1982, the CDC revised its definition of AIDS. It now classified a case of AIDS "as a disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease. Such diseases include KS [Kaposi's sarcoma], PCP [*Pneumocystis carinii* pneumonia], and serious OOI [other opportunistic infections]." The CDC noted, however, that the case definition may not include the full spectrum of manifestations that preceded the development of full-blown AIDS. These manifestations ranged from the absence of symptoms, despite laboratory evidence of immune deficiency; to non-specific symptoms (such as fever, weight loss, and generalized, persistent lymphadenopathy); to specific diseases (such as tuberculosis, oral candidiasis, and herpes zoster). By that time, 593 cases of AIDS had been reported to the CDC, 243 of them fatal. As reported by the CDC, 75 per cent of the persons involved were homosexual or bisexual men, 13 per cent were intravenous drug users, 6 per cent were Haitians, 0.3 per cent were hemophiliacs, and the remainder did not belong to any of those risk groups.

In that month, September 1982, the CDC reported that "the epidemiology of AIDS suggests an unidentified and uncharacterized blood-borne agent as a possible cause of the underlying immunologic defect." A report in the scientific journal *Nature* concluded that the "apparent transmission [of AIDS] by sexual contact, drug apparatus and blood products strongly suggest[s] a viral agent." At a meeting of the Food and Drug Administration's blood products advisory committee that month, Dr Evatt described five hemophiliacs diagnosed with AIDS, or with signs and symptoms consistent with the precursor states of AIDS, and warned that the factor concentrates used by hemophiliacs might be an agent of transmission. The minutes record that the committee concluded that although "it was useful for the committee

and the staff of the Office of Biologics to remain current on the issue ... there are insufficient data to suggest that any immediate action [be taken] with licensed blood products."

In October, the CDC began to receive anecdotal reports of newborn infants with unexplained immunologic abnormalities whose parents were either Haitian or consistent users of illegal drugs. In the same month, opportunistic infections were reported in five women in New York City, four of whom were drug users; the fifth did not use drugs but had a sexual partner who was a drug user, raising the "possibility that the syndrome can be acquired by intimate heterosexual contact." In an article discussing these five cases, Dr Henry Masur and colleagues said in the *Annals of Internal Medicine* that "[t]he extension of this outbreak to women has important implications concerning the cause, pathogenesis, and mode of transmission of this new syndrome, and should alert the medical community to consider the spread of this outbreak to new populations." Also in October, the National Hemophilia Foundation recommended that homosexual men, intravenous drug users, and Haitians be excluded from donating blood or plasma in circumstances in which the plasma from the donations could be used to manufacture factor VIII or factor IX concentrates.

In November 1982, the CDC published recommendations for clinical and laboratory workers dealing with AIDS patients. Because the epidemiological patterns of AIDS and hepatitis B were similar, it recommended that clinical workers use the same precautions in caring for patients with AIDS as were standard in caring for patients with hepatitis B. The clinical and laboratory workers were told that

blood and body fluids likely to have been contaminated with blood [should be] considered infective. Specifically, patient-care and laboratory personnel should take precautions to avoid direct contact of skin and mucous membranes with blood, blood products, excretions, secretions, and tissues of persons judged likely to have AIDS.

The CDC also recommended that AIDS patients not be permitted to donate blood or organs. By the end of November, 744 cases of AIDS had been reported in the United States, the CDC was investigating a sixth case of AIDS in a hemophiliac, and investigations were continuing into possible cases of AIDS among infants.

Dr Evatt reported to the Food and Drug Administration's blood products advisory committee on 4 December that the epidemic was growing at an almost exponential rate, doubling every six months; that the incubation period from exposure to the development of precursor conditions was approximately four to seven months; that the period from the development of precursor conditions to the diagnosis of AIDS was another four to seven months; and that the epidemiological pattern was similar to that of hepatitis B. Of the

788 cases then reported, eight were hemophiliacs and five were persons who had received blood transfusions; Dr Evatt expressed a concern that transfusion cases "may follow the same increasing pattern seen with hemophilia patients." The minutes record "a sense of urgency because of the continuing spread of AIDS and because of its long incubation time." At this meeting, Dr Lewellys Barker, the vice-president of health services of the American Red Cross, said that while there was as yet no proof, "it looks very much as if [AIDS] is caused by a transmissible agent." The committee discussed immediate steps that could be taken to reduce the risk of AIDS transmission in blood and blood products. These measures included relying on cryoprecipitate rather than on factor concentrates in treating hemophilia, because of the greatly reduced risk of contamination; developing methods of processing that would reduce the likelihood of infection from blood products; excluding donors at high risk for the disease; and carrying out additional routine tests to screen for markers of infection in donated blood and plasma. The committee made no recommendations, pending further investigation and study.

The *Morbidity and Mortality Weekly Report* of 10 December 1982 reported that the hemophiliac AIDS patients whose cases had been reported in July had since died. It also reported four more cases of opportunistic infections in hemophiliacs and one suspected case that did not meet the strict criteria for AIDS. (The suspected case involved a seven-year-old hemophiliac with symptoms slightly different from those of other cases, and the CDC had not yet settled on a definition of pediatric AIDS.) These newly diagnosed patients, like the three original hemophiliacs who were diagnosed with AIDS, lived in disparate geographical regions and had been treated with different lots of factor VIII concentrate. The CDC said that the number of hemophiliacs with AIDS was continuing to increase, and that patients with hemophilia might be at significant risk of contracting AIDS. The National Hemophilia Foundation told its members of the new cases. It said that while "there is insufficient data to directly link the spread of AIDS to concentrates, there is an increased concern that AIDS may be transmitted through blood products." Although it did not describe the potential risks, it counselled patients and parents to be aware of them.

The *Morbidity and Mortality Weekly Report* of 10 December 1982 also included the first published report of AIDS related to a blood transfusion. A twenty-month-old infant in San Francisco had died after receiving a transfusion of blood from a donor who subsequently developed AIDS. This case was significant for several reasons. Both the donor and the recipient had AIDS. The incubation period from receipt of the blood until the onset of AIDS could be established, and was approximately a year and a half. The donor had no symptoms of AIDS at the time of donation. These circumstances lent strong support to the theory that AIDS might be caused by an infectious agent transmitted through exposure to blood and blood products. A newsletter published by the Council of Community Blood Centers the same day also said that

the cases described in these two articles suggested "the possibility that an infectious agent capable of causing AIDS may be transmissible by transfusion of blood products derived from affected donors." In response, the National Hemophilia Foundation issued new guidelines to its members for the treatment of hemophilia. It recommended that factor concentrates not be given to persons who had had little or no exposure to factor concentrates. These persons included children under four years of age, patients newly diagnosed with hemophilia, and patients with mild hemophilia.

The "California baby case," as it came to be known, was important. It not only provided strong evidence that AIDS was transmitted by blood, but it also demonstrated that infected persons could transmit the disease even though they had not yet developed the symptoms of AIDS. At this time it was not known whether all those infected would develop AIDS.

On 17 December, the CDC reported that AIDS had been diagnosed in four children born to mothers who were prostitutes, Haitian, or intravenous drug users, suggesting the possibility of transmission from mother to child, either *in utero* or shortly after birth. During December, the CDC also received two reports of immunodeficiency in heterosexual women whose only risk factor was that their male partners had AIDS. They were reported in the *Morbidity and Mortality Weekly Report* of 7 January 1983, with the comment that the "report supports the infectious agent hypothesis and the possibility that transmission of the putative 'AIDS agent' may occur among both heterosexual and male homosexual couples."

In December 1982, Dr Foege reported to a congressional subcommittee concerned with health matters that there were seven "definite cases" of AIDS in hemophiliacs, one "highly suspicious" case and several cases under investigation. There were also three cases of AIDS in recipients of blood transfusions. Dr Foege told the subcommittee that the "current prevailing theory is that AIDS is caused by a virus which is similar to hepatitis B." By that time, more than 800 cases of AIDS had been reported in the United States.

Some persons working closely with the disease within the CDC considered the evidence that AIDS was transmitted by a blood-borne viral agent to be persuasive. Other agencies and organizations remained sceptical, but some scientists in the CDC were persuaded by several factors. The first was the diagnosis of AIDS in recipients of blood transfusions who were not members of any group identified as at risk. Next, the other apparent modes of transmission – through sexual contact among homosexual men, through sharing of needles among intravenous drug users, through heterosexual contact among drug users and their partners, and through the use of factor concentrates by hemophiliacs – mirrored those of hepatitis B. Finally, the diagnosis of AIDS in hemophiliacs suggested not only that the causal agent was infectious and blood borne, but also that it was a virus – because only viruses would not be filtered out during the purifying process to which blood products were then subjected.

Early in December, officials from the CDC, the Food and Drug Administration, and the National Institutes of Health held a conference call to discuss the articles on transfusion-associated AIDS that would soon appear in the *Morbidity and Mortality Weekly Report* and to consider what action should be taken. They decided to establish an ad hoc advisory group on AIDS that would report to the assistant secretary for health, recommending methods of reducing the risk of AIDS transmission through blood and blood products. A meeting was scheduled for 4 January 1983 with three purposes: to alert persons working within the national blood system to the fact that AIDS might be transmissible by blood, to coordinate efforts among agencies of the Public Health Service, and to formulate recommendations.

More than 200 persons were present at that meeting. Most had attended the Washington meeting on 27 July 1982. The Public Health Service was represented by employees of the CDC, the Food and Drug Administration, and the National Institutes of Health. Also present were representatives of the blood and plasma centres, the four large U.S. blood product manufacturers, the gay community, and the National Hemophilia Foundation, and some treating physicians.

Dr Evatt opened the meeting by presenting evidence suggesting that AIDS could be transmitted by blood. He discussed the cases of AIDS seen in hemophiliacs, described the case of an infant who had received a transfusion at birth, and said that five unconfirmed cases of transfusion-associated AIDS were still being investigated. He also pointed out that the epidemiological pattern of AIDS was similar to that of hepatitis B, a blood-borne virus. According to the official record of the meeting, "[s]ome participants were reluctant to accept the hypothesis that AIDS has been transmitted by whole blood in the absence of additional evidence."

Several measures were suggested to reduce the risk of transmission. Dr Francis, the CDC virologist, advocated direct questioning of blood donors about behaviour that would have placed them at risk of contracting AIDS. He also recommended that donations be tested for the presence of antibody to the core antigen of hepatitis B virus, in the belief that persons who had been exposed to hepatitis B would also be at greater than normal risk of contracting AIDS. Representatives of the gay community objected to his first proposal because it would be discriminatory; representatives of the blood banks and plasma industry objected to the second, primarily because it would be too expensive. Dr Oscar Ratnoff, a physician who treated hemophiliacs, recommended that hemophiliacs be treated with cryoprecipitate instead of factor concentrates. Ultimately, the meeting endorsed none of these measures. Although the participants reached a consensus that "it would be desirable to exclude high-risk donors to reduce the risk of AIDS transmission," there was no agreement about a method of accomplishing that goal. There was also no consensus on the question whether AIDS was caused by a transmissible agent, on the risk of AIDS from blood donations, or on the desirability

of introducing new methods of donor screening or testing to reduce the risk of transmission. Instead, the CDC, the Food and Drug Administration, and the National Institutes of Health were each asked to submit a set of recommendations, after the meeting, for the prevention of AIDS in patients with hemophilia and for other recipients of blood and blood products so that a uniform set of recommendations might be developed. These recommendations were announced by the Department of Health and Human Services on 4 March 1983. Although they were not binding on blood banks, their principles were endorsed three days later in a joint statement by the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers. Members of groups at high risk of contracting AIDS were to be urged to refrain from donating blood or selling plasma, in part by information given at the collecting site. High-risk groups were identified as persons with AIDS, sexual partners of persons with AIDS, persons with symptoms and signs suggestive of AIDS, sexually active homosexual or bisexual men with multiple partners, Haitian entrants to the United States, present or past users of intravenous drugs, and sexual partners of individuals at high risk of contracting AIDS.

The transmission of AIDS continued to be a concern of the Public Health Service throughout 1983. Early in the year, the National Institutes of Health established an interagency agreement with the CDC to evaluate immunologic changes in hemophiliacs and in patients who had received transfusions. In March, the assistant secretary for health, Dr Edward Brandt, established an executive committee on AIDS to coordinate the activities of Public Health Service agencies and to exchange information on future meetings, grants, and developments. Dr Brandt also directed the National Institutes of Health to support studies evaluating the effectiveness of various laboratory tests to identify and exclude donations of blood or plasma from members of high-risk groups. In May, the Department of Health and Human Services announced that the Conference of State and Territorial Epidemiologists had passed a resolution that AIDS should become a notifiable disease. Physicians and health care institutions were urged to report cases to their state health departments.

During 1983, evidence that AIDS could be transmitted by both blood and blood products continued to accumulate. On 7 January 1983, the CDC published a report of sixteen cases of AIDS in prison inmates who had a history of intravenous drug use. It said that "[s]ince male homosexuals and IV [intravenous] drug abusers are known to be at increased risk for AIDS the occurrence of AIDS among imprisoned members of these groups might have been anticipated." In May, several articles published in *Science* suggested that AIDS was caused by a retrovirus. In its issue of 20 May 1983, it reported that Dr Luc Montagnier and his colleagues at the Pasteur Institute in Paris had successfully isolated an agent they called the lymphadenopathy-associated virus (LAV) from the lymph gland of an infected homosexual man.

In November 1983, the *Annals of Internal Medicine* reported a second case of transfusion-related AIDS, that of a heterosexual man who had received sixteen units of whole blood and plasma during coronary artery bypass surgery and who developed *Pneumocystis carinii* pneumonia twenty-nine months later. By December 1983, twenty-one cases of AIDS had been reported among persons with hemophilia.

In January 1984, the *New England Journal of Medicine* published a summary of eighteen cases of AIDS, none of which involved any risk factors other than receipt of blood components within five years of the onset of the illness. Based on these investigations, the authors concluded that "exposure to as little as one unit" might result in transmission of AIDS. Many persons involved in transfusion medicine were aware of this article before its publication and were persuaded by the evidence. As Dr Thomas Zuck, a former director of the division of blood and blood products in the U.S. Food and Drug Administration, said in his testimony, "everyone knew about this paper months before it showed up. It was widely circulated that this was coming out; it was of concern to the blood bankers because it was likely to get press play, which it did. It was likely to frighten patients." Dr Zuck went on to say that the article "put the whole medical community and perhaps the world on notice that AIDS is transmitted by blood transfusions," and that by January 1984 "the debate [was] over."

In a press conference with Dr Robert Gallo in late April 1984, the U.S. Secretary for Health and Human Services announced that the probable cause of AIDS had been found. In May 1984, *Science* published an article by Dr Gallo and his colleagues that contained strong evidence that AIDS was caused by a virus, the human T-lymphotropic virus III, or HTLV-III (subsequently called the human immunodeficiency virus, or HIV). This was the same type of virus as that isolated by Dr Luc Montagnier one year earlier from the lymph gland of a person with AIDS.

10

Canada's Early Response to the Emergence of AIDS

In February 1982, the Laboratory Centre for Disease Control, which conducted disease surveillance on behalf of the Government of Canada, received the first report of a case of AIDS in Canada. By 6 August, eight cases had been reported, and six of the persons had already died. By 2 October, the Laboratory Centre had received information about twelve cases and three suspected cases. By this time, other Canadians were suffering from the early signs of AIDS; their condition did not meet the formal definition of the syndrome that had been formulated by the U.S. Centers for Disease Control, although many were being watched carefully by their physicians. A group of Montreal physicians, for example, were aware of as many as twenty-seven possible cases of AIDS in that city, and in Vancouver physicians were following more than fifty homosexual men who had lymphadenopathy, a condition associated with the later development of AIDS in some persons.

The Canadians who developed AIDS in 1982 belonged to the same risk groups as in the United States. The first reported case was that of a homosexual man who died of *Pneumocystis carinii* pneumonia. Of the twelve cases reported by October, five of the persons had been born in Haiti and had been in Canada for four years or less and seven were homosexual men. The mortality rate in Canada was high, as in the United States; nine of the twelve persons whose cases were reported in October had already died.

In the United States, the Centers for Disease Control had established a task force on AIDS in June 1981. During the first year after the appearance of AIDS in Canada, the Canadian response, including surveillance for the presence of the disease, was guided by a small group of epidemiologists at the Laboratory Centre for Disease Control.

Early responses by federal and provincial health authorities

The Bureau of Epidemiology, a division of the Laboratory Centre for Disease Control, began watching for appearances of what came to be known as AIDS soon after the first report was published in the United States, in June 1981, of *Pneumocystis carinii* pneumonia in five homosexual men. Following the practice of the U.S. Centers for Disease Control, the bureau reviewed provincial

tumour registries and records of laboratories and venereal disease clinics for reports of Kaposi's sarcoma, *Pneumocystis carinii* pneumonia, and cytomegalovirus infections. It focused its efforts on Montreal, Toronto, and Vancouver, which were known to have large homosexual populations. It discovered no cases.

Not all the early measures taken in the United States to monitor the spread of AIDS were pursued in Canada. For example, there was in Canada no systematic communication during 1981 or 1982 with the heads of the infectious disease, dermatology, oncology, and pathology departments of major hospitals, or with physicians who were treating sexually transmitted diseases in the gay community. These physicians were well known to members of the Bureau of Epidemiology, but, as Dr Gordon Jessamine, the chief of its Field Epidemiology Division, testified, "with the [low] numbers [of AIDS cases] we had on hand at that particular time, it would have been considered a rather fruitless piece of work considering the volume of non-AIDS work that was still pending on our desks."

The Bureau of Epidemiology assumed, however, that cases of AIDS inevitably would appear in Canada. "I think it's only a matter of time," Dr Jessamine said during an interview reported in early February 1982. When he made the prediction, Dr Jessamine did not know that the Centers for Disease Control had recently linked a Canadian flight attendant to several cases of AIDS in New York and California. The flight attendant had travelled extensively to the gay urban centres of Canada and the United States between 1979 and 1983.

The Laboratory Centre for Disease Control received its first report of a case of AIDS later in February. The person involved lived in Windsor. He had visited homosexual communities in Toronto, New York, and San Francisco, and had become ill shortly after a trip to Haiti. A report of this case was published in the *Canada Diseases Weekly Report* of 27 March 1982. It was accompanied by an editorial comment that summarized developments since the first cases had been identified in the United States, including the rapid rise in their number, the groups most affected, and the pathogens and diseases commonly associated with immunosuppression. The editorial comment included a passage from a special report by the Centers for Disease Control, noting that

[t]he simultaneous occurrence of Kaposi's sarcoma and P. [neumocystis] carinii pneumonia among homosexual men of the same age and racial groups who live in the same geographical areas strongly suggests the occurrence of a single epidemic of underlying immunosuppression in these men. If immunosuppression is the underlying cause of these conditions, then Kaposi's sarcoma and P. carinii pneumonia may represent the "tip of the iceberg" including other conditions that are less readily recognized or have longer latency periods.

In the editorial comment, the bureau asked physicians for the first time to report cases of the new syndrome to it, and asked for "any information on immunosuppression and associated diseases in homosexuals in Canada."

Special forms for reporting cases of AIDS in Canada were not drafted until August 1982. A month earlier, Dr Jessamine had sent a copy of a form that had been created for this purpose by the U.S. Centers for Disease Control to the provincial epidemiologists of at least four provinces – Ontario, Quebec, British Columbia, and Alberta. The covering letter told them how to report cases to the Centers for Disease Control in Atlanta and asked them to send "copies of completed forms" to the Laboratory Centre for Disease Control in Ottawa. It gave no directions or suggestions for the further distribution of the form or about other surveillance measures that might be undertaken in the provinces. Dr Jessamine testified that he expected that the provincial public health authorities would conduct their own surveillance. However, they made very few efforts to monitor the spread of AIDS until 1983. What was done was conducted in large part by physicians.

In the late summer of 1982, the AIDS Committee of Montreal, whose members were physicians, was established under the auspices of the local regional program for the control of sexually transmitted diseases. The committee reviewed the cases of twenty-seven persons suspected of having AIDS, many of whom had already died. In Vancouver, a group of physicians practising in the west end of the city, where many homosexual men lived, made some of the earliest efforts at surveillance by meeting informally to discuss the increasing number of patients who had persistent lymphadenopathy. By November 1982, they had identified more than fifty persons with this condition, although only three had been diagnosed as having AIDS. Another group of physicians, at the Cancer Control Agency of British Columbia in Vancouver, began monitoring the spread of AIDS soon after they had read the first published report, in July 1982, of AIDS among hemophiliacs in the United States. They established a committee that consisted of members of the agency, the provincial public health laboratories, and the Canadian Red Cross Society (Red Cross), along with physicians who were treating infectious diseases, including one member of the west end group. This committee was eventually replaced by a provincial advisory committee on AIDS established by the provincial Ministry of Health.

In December 1982, the Laboratory Centre for Disease Control published a list of precautions in its *Canada Diseases Weekly Report* for laboratory and hospital personnel caring for AIDS patients. These recommendations originally appeared in the *Morbidity and Mortality Weekly Report*, a publication of the U.S. Centers for Disease Control, of 5 November 1982. They were premised on the view that AIDS was caused by an infectious blood-borne pathogen – a "hypothesis consistent with current observations," as said by the Centers

for Disease Control. The Laboratory Centre's advice included the recommendation that blood and other specimens taken from suspected AIDS patients be labelled "Blood Precautions" or "AIDS Precautions."

The response to the first report of AIDS among hemophiliacs

On 16 July 1982, the Centers for Disease Control published a report in their *Morbidity and Mortality Weekly Report* of three hemophiliacs in the United States who had been diagnosed with *Pneumocystis carinii* pneumonia. An editorial note accompanying the report said that "[a]lthough the cause of the severe immune dysfunction is unknown, the occurrence among the three hemophiliac cases suggests the possible transmission of an agent through blood products."

By July 1982, most severe hemophiliacs in Canada were routinely using coagulation factor concentrates. Approximately half the concentrates they used were manufactured in the United States from plasma collected from paid donors in that country. If the same concentrates were transmitting an infectious, fatal disease in the United States, the Canadian hemophiliacs who used them likely were exposed to the same risk. The other factor concentrates used in Canada, manufactured from plasma obtained from Canadian donors, were also not risk-free. They were known to transmit hepatitis, another blood-borne infectious disease, but many experts believed that they were less likely than the U.S. concentrates to cause AIDS because Canadian donors were not paid. Several studies had demonstrated that purchased plasma was more likely to be contaminated than voluntarily donated blood and plasma. However, AIDS had begun to emerge in the Canadian population and, if infected individuals were donating blood, their blood and the products manufactured from it were also likely to be contaminated.

Dr Jessamine, recognizing the potential risk to Canadian hemophiliacs, telephoned the Red Cross on 3 August 1982 to discuss the report of AIDS-infected hemophiliacs in the United States. Dr John Derrick, the director of blood products services, told him that the Red Cross had received no reports of AIDS or related infections in recipients of blood or blood products, but his office had held informal discussions with physicians who worked with hemophiliacs, and the Red Cross was maintaining a "watching brief." Dr Jessamine made a similar call to Connaught Laboratories Limited, the only Canadian manufacturer of factor concentrates, which also said that it had received no reports of AIDS in recipients of its products. At about the same time, Dr Jessamine contacted the Canadian Hemophilia Society, which was pursued further in September. He did not contact the U.S. fractionators whose blood products were distributed in Canada. Dr Jessamine testified that he was not then aware that Canadian hemophiliacs used some of the same factor concentrates that were distributed in the United States.

An advance copy of the report in the issue of the *Morbidity and Mortality Weekly Report* dated 16 July was mailed to Dr John Furesz, the director of the Bureau of Biologics, which licensed and otherwise regulated all factor concentrates distributed in Canada. On 27 July 1982, the U.S. Public Health Service sponsored an open meeting in Washington, DC, to discuss the occurrence of opportunistic infections in patients with hemophilia. The bureau later received a copy of the summary report of this meeting. Dr Furesz was aware that Canadian hemophiliacs used significant quantities of commercial factor concentrates manufactured in the United States. He approached the Red Cross, the sole distributor of factor concentrates in Canada, to ask for its help in monitoring the incidence of the disease among hemophiliacs. He did not contact the manufacturers whose products were licensed by the bureau for distribution in Canada and who were the primary sources of information about the occurrence of adverse reactions, including the transmission of infectious disease, among the users of their products.

The Canadian Red Cross Society

On 4 August 1982, Dr Furesz asked the Red Cross to coordinate surveillance activities related to AIDS and hemophiliacs. The Red Cross was asked to tell physicians about AIDS and establish procedures for physicians to report cases of AIDS to the Red Cross. He also asked the Red Cross to establish a procedure for the laboratory investigation of cases that were reported.

In a memorandum dated 13 August 1982, Dr Derrick reported to the national director and assistant national director of the Red Cross blood transfusion service:

He [Dr Furesz] was aware that Dr. Jessamine had discussed the U.S. reports with me and had followed that up with CHS [Canadian Hemophilia Society] contacts. Dr. Furesz stated that in this instance, however, he was "wearing his regulatory hat" and was officially requesting the assistance of CRC BTS [Canadian Red Cross blood transfusion service] in alerting, through our Centres, all physicians who might be using intravenously administered blood products of the possible occurrence of Acquired Immune Deficiency Syndrome (AIDS) and resultant opportunistic infection.

Later that month, Dr Derrick told Dr Furesz that he would prepare an outline of a request to the medical directors of the Red Cross's seventeen local blood centres and to physicians who were treating hemophiliacs, asking them to report to the Red Cross suspected cases of opportunistic infections in hemophiliacs.

Dr Derrick reported his discussions with Dr Furesz to the immunology-virology working group, an internal committee of the Red Cross's blood transfusion service, when it met on 9 September 1982. Dr Furesz, he said, had

asked that the Red Cross medical directors "be alerted to the possibility that hemophiliacs may constitute a high-risk group susceptible to the development of AIDS." The working group, according to the minutes, believed that "the evidence suggesting that hemophiliacs could be at risk in developing AIDS had been overpublicized and was still inconclusive." It resolved, however, that "a cooperative approach between the CRC BTS [Canadian Red Cross blood transfusion service] and the Canadian Hemophilia Society should be adopted with respect to requesting information on the identification of any Canadian hemophilia patients who develop AIDS."

The Red Cross soon decided that it could not play the central role in AIDS surveillance that Dr Furesz had requested. There were several reasons for the decision: cases of AIDS could appear anywhere in the health system; the collection of epidemiological data was the task of public health agencies; and other organizations, such as the provincial colleges of physicians and surgeons, were in a better position to communicate with physicians. The Red Cross might also have been influenced by a decision of the American Red Cross in September 1982 not to take an "active position on AIDS" because it was "felt that evidence of a direct or causative involvement of blood products in the development of the syndrome is very slim." Dr Martin Davey, then the assistant national director of the Red Cross blood transfusion service, testified that, while the Red Cross was willing to cooperate with whatever surveillance system was established, it was inappropriate to assign to it the primary responsibility for the system's development and administration. Later, the Red Cross did agree to encourage the reporting of cases of AIDS through its blood centres.

In responding to the second aspect of Dr Furesz's request, Dr Derrick met on 10 August 1982 with members of the staff of the Central Ontario Public Health Laboratory who had had experience in investigating opportunistic infections. Dr Derrick was accompanied by Dr Derek Naylor (the deputy director of the Red Cross's blood products services) and a member of the Red Cross's national reference laboratory. A procedure was drafted for testing samples from persons reported to have opportunistic infections. A month later, however, Dr Derrick reviewed the literature about AIDS and realized that the procedure was inappropriate. It had been designed in the belief that the deficiencies in the immune response of patients with AIDS were humoral (that is, in the antibodies and other proteins carried in the blood) rather than cellular (that is, in cells such as lymphocytes that are carried in the blood).

The Red Cross, during a meeting on 27 September 1982, reported that it could not comply with Dr Furesz's requests. Representatives of the Bureau of Biologics, the Laboratory Centre for Disease Control, the Red Cross, and the Canadian Hemophilia Society attended this meeting, which had been

called to discuss "the occurrence, reporting and verification of ... AIDS with particular reference to recipients of blood and blood products," and to co-ordinate surveillance activities for AIDS. Dr Derrick's report of the meeting contained the following summary:

I covered the problems I had encountered in following up on Dr Furesz's request that the CRC [Canadian Red Cross] Centre Medical Directors be alerted to the possibility of AIDS cases occurring in their various regions and that cases be reported to CRC National Office and from there to BoB [Bureau of Biologics]. The problems were based on the following factors:

- a. that the evidence that blood and blood products were involved in the development of AIDS was inconclusive;
- b. that CRC was not in a position to initiate a reporting system, verification of reported cases and possible coordination of specimen testing;
- c. that with current evidence that the immunosuppression was at the cellular rather than the humoral level most of the testing protocol which the Ontario Public Health Laboratory ... and we had been able to put together ... was no longer relevant.

Dr Derrick's report stated that Dr Furesz expressed his appreciation of the Red Cross's efforts to respond to his requests, but that he "would still like to see the introduction of an AIDS reporting system" and that he "felt it was still worthwhile to consider development of a testing profile" to identify groups vulnerable to AIDS. Dr Furesz, he said, suggested that cases of AIDS should be reported on a special form prepared by the Laboratory Centre for Disease Control, which was then being reviewed by the Red Cross and the Canadian Hemophilia Society.

In December 1982, the Red Cross national office sent the medical directors of its blood centres information about AIDS and a copy of the form prepared by Dr Jessamine for reporting cases to the Laboratory Centre for Disease Control. A covering letter stated:

Your cooperation in encouraging in your region the reporting of cases in which the AIDS is a possibility, particularly those where blood products could be involved, is earnestly solicited.

Dr Davey should receive copies of reports on cases where blood product involvement is a possibility.

From the medical directors, the information was expected to pass to hospitals and frequent users of blood and blood products.

The Canadian Hemophilia Society

On 23 July 1982, Dr Hanna Strawczynski, the chair of the Canadian Hemophilia Society's medical and scientific advisory committee, received a copy of a newspaper article about the "gay plague" and a copy of the report of 16 July by the Centers for Disease Control about the three U.S. hemophiliacs who had been diagnosed as having AIDS. On 20 August, she sent a memorandum to "All Directors of Hemophilia Centres," enclosing copies of the report and a related "patient alert" that had been distributed by the U.S. National Hemophilia Foundation on 14 July. In the memorandum, she said that she had discussed the report with the past chairs of the medical and scientific advisory committee. "Obviously," she wrote, "we should avoid causing unnecessary anxiety – this has already been done by some newspaper reports. On the other hand, our patients should be informed and they must not feel that information is being withheld from them." Dr Strawczynski left it to the clinic directors "to decide how [the enclosed] material should be communicated to your patients." Dr Strawczynski testified that her immediate concern had been to allay anxiety among hemophiliacs, which she feared would cause them not to treat their bleeding episodes appropriately. She also testified that the primary responsibility for giving hemophiliacs information relevant to their treatment lay with their physicians, and not with the Canadian Hemophilia Society or its medical and scientific advisory committee. The approach proposed by Dr Strawczynski in her memorandum of 20 August was endorsed by the medical and scientific advisory committee when it next met, on 16 September 1982.

When it first learned of the appearance of AIDS among hemophiliacs, the Centers for Disease Control had immediately enlisted the assistance of the National Hemophilia Foundation in warning hemophiliacs and their physicians about AIDS and in developing a system for reporting AIDS and AIDS-related symptoms among hemophiliacs. Dr Jessamine discussed the report in the *Morbidity and Mortality Weekly Report* with Dr Strawczynski in early August, but no specific discussions about the Canadian Hemophilia Society's participation in a surveillance system occurred until 13 September. On that day, Dr Strawczynski told Dr Jessamine about what she suspected was the first case of AIDS involving a Canadian hemophiliac. During their conversation, a procedure was established for reporting and monitoring the incidence of AIDS among Canadian hemophiliacs. Dr Strawczynski agreed to distribute the questionnaire that had been prepared by the Laboratory Centre for Disease Control to hemophilia treatment centres throughout Canada. It was also agreed that the Laboratory Centre and the Canadian Hemophilia Society would continue to exchange information.

It was only after his discussion with Dr Strawczynski that Dr Jessamine learned that Dr Furesz, the director of the Bureau of Biologics, had asked the Red Cross some six weeks earlier to establish a system for the surveillance

of AIDS among hemophiliacs. The Bureau of Biologics and the Laboratory Centre for Disease Control, in which Dr Jessamine worked, were both agencies of the Health Protection Branch and had offices in the same building in Ottawa. On 14 September, one day after his discussion with her, Dr Jessamine wrote to Dr Strawczynski as follows:

Dr. John Furesz, Director, Bureau of Biologics, Health and Welfare Canada, has since advised me that he, in collaboration with Dr. Derrick of the Canadian Red Cross has instituted a surveillance and reporting system for AIDS cases in haemophiliacs in Canada. You may therefore wish to contact Dr. Derrick directly. It is obviously redundant to have two reporting and surveillance systems. I am sure that you and your colleagues will select the most appropriate one to serve your interests. Despite this, the Bureau of Epidemiology would appreciate receiving copies of the information you collect on haemophiliac cases in order to maintain our overall surveillance of AIDS in Canadians.

With his letter, Dr Jessamine enclosed a copy of the form prepared by the Laboratory Centre for Disease Control for the reporting of all suspected cases of AIDS. He acknowledged in the letter that it might be "inadequate for surveillance of haemophiliac cases and for reporting specific factors in these cases." He suggested that Dr Strawczynski might find of "greater value" a form that had been created by the U.S. Centers for Disease Control specifically for reporting AIDS among hemophiliacs. The Laboratory Centre for Disease Control's form was not designed to collect specific information about hemophiliacs. It was to be completed only following a diagnosis of AIDS from the presence of certain indications such as Kaposi's sarcoma or *Pneumocystis carinii* pneumonia. The form prepared by the Centers for Disease Control, with the assistance of the U.S. National Hemophilia Foundation, asked physicians to report not only cases of AIDS, but also cases of hemophiliacs who had "non-specific" signs and symptoms that fell short of the formal definition of AIDS but had come to be associated with the precursor stage of the disease. The U.S. form also asked for information about the type and quantity of blood products used by the patient – data needed for assessing the relative risk of various coagulating factor replacement therapies. The Canadian form did not seek information of that nature.

Dr Jessamine advised Dr Furesz of what he had written to Dr Strawczynski and added:

I have advised her ... that she should get in touch with Dr Derrick on this point. Between them they can sort out a system which will be helpful to us all – whether it be a Canadian or CDC system format.

Like you, I don't mind what they tell us, as long as they tell us! Therefore I have suggested that she photocopy information she sends out, to LCDC.

Dr Jessamine testified that he had had no objection to Dr Furesz's approach to the Red Cross as long as he was kept informed of all cases of AIDS that were reported.

When the medical and scientific advisory committee of the Canadian Hemophilia Society met on 16 September, Dr Strawczynski reviewed the current information about AIDS. The minutes record that "the possibility was raised of an immunosuppressive agent, possibly a virus, being transmitted in blood products." Dr Strawczynski reported that she was already aware of one hemophiliac in Montreal who showed immune abnormalities similar to those found in patients with AIDS. The committee decided not to send a patient alert similar to the one that the National Hemophilia Foundation had sent to hemophiliacs and their physicians in the United States two months earlier. Instead, Dr Strawczynski was to prepare a short informative article for *Hemophilia Today*, the quarterly publication of the Canadian Hemophilia Society. Dr Strawczynski promptly drafted the article for *Hemophilia Today*, but it did not appear in the September issue. In December 1982, the National Hemophilia Foundation recommended that, although there was no conclusive evidence that cryoprecipitate and fresh frozen plasma were safer than concentrates, persons who had never used concentrates not begin using them. Dr Strawczynski's article appeared in the January 1983 issue of *Hemophilia Today*. By the time the article appeared, it was, to use Dr Strawczynski's word, "obsolete"; it did not recommend any change in the use of blood products.

During its meeting on 16 September, the medical and scientific advisory committee also discussed procedures for the surveillance and reporting of cases of AIDS. It was agreed that, regardless of which of the two forms was used, physicians treating hemophiliacs would report cases of AIDS to the Laboratory Centre for Disease Control, which would in turn report them to the Centers for Disease Control in Atlanta. The physicians were to send copies of the completed forms to Dr Strawczynski. Dr Strawczynski gave different instructions later, when she distributed copies of the Laboratory Centre's form to members of the committee and the directors of hemophilia clinics. She said that reports on the Laboratory Centre's form were to be sent to Ottawa, but reports on the Centers for Disease Control's hemophilia-specific form, which would be distributed in the future, were to be sent directly to Atlanta. After issuing those instructions, Dr Strawczynski attended a meeting on 27 September with representatives of the Red Cross, the Laboratory Centre for Disease Control, and the Bureau of Biologics. There she agreed with "the concept of a uniform system of reporting the diseases regardless of the clinical group to which a patient might belong" and said that the Canadian Hemophilia Society found the Laboratory Centre for Disease Control's reporting form "acceptable." However, no further instructions were sent to physicians treating hemophiliacs about which form to use or where completed forms were to be sent.

The existence of two reporting forms, with inconsistent instructions as to how they should be used, created confusion and impeded the collection of reliable data. Dr Strawczynski testified that she could not recall having received a single copy of any reported case, on either form, at any time while she was the chair of the medical and scientific advisory committee. In September 1983 she again asked the members of the advisory committee to send her copies and reported that "As far as I know, there are no new cases of AIDS among hemophiliacs and the count in Canada is 2. However, this may not be so, since our reporting system does not work well. Please notify me about any case, suspected or proven." In December 1983 she wrote to her colleagues that "at the risk of sounding repetitious, I have to remind you that I have not received any information from you, and that our reporting system is non-existent."

Canadian surveillance studies of AIDS among hemophiliacs

In the United States, in addition to the joint surveillance efforts of the Centers for Disease Control and the National Hemophilia Foundation, the occurrence of AIDS and AIDS-related symptoms among hemophiliacs was monitored in several small studies conducted by regional hemophilia programs, assisted financially by the U.S. Public Health Service. By late 1982 and early 1983 these studies had revealed that a large proportion of hemophiliacs showed signs of immune dysfunction and that this phenomenon was more common among moderate and severe hemophiliacs who used large amounts of factor concentrates than among those who continued to use cryoprecipitate.

The importance of similar studies in Canada was recognized. When they met on 10 August 1982, representatives of the Red Cross and the Central Ontario Public Health Laboratory had discussed a pilot study involving 100 patients with type A hemophilia. The need for a study was discussed again during the meeting on 27 September at which the Red Cross said it could not coordinate the surveillance program. According to Dr Derrick's record of the meeting, Dr Furesz "felt quite keenly" that a Canadian study should be undertaken of a group at risk of contracting AIDS and singled out, as an example, hemophiliacs receiving blood products. It was agreed that the Red Cross and the Canadian Hemophilia Society would "attempt to facilitate a study to assess groups at risk of developing AIDS in which it may be possible to include a group of hemophiliac patients"; that medical and scientific groups interested in such a study would be approached; and that emergency funding for the study would be sought from the Medical Research Council, a federal granting agency.

Dr Derrick invited physicians from the Toronto General Hospital and the Hospital for Sick Children to an ad hoc meeting on 13 October 1982 to discuss such a study. At the suggestion of Dr Furesz, he also invited Dr Alastair Clayton, the director general of the Laboratory Centre for Disease Control.

The group recognized that AIDS posed a serious health problem in Canada and believed, according to a Red Cross record of the meeting, that the expertise, and some of the necessary laboratory research techniques, were already in place. However, an estimated \$100,000 would be needed to develop and coordinate the work.

Dr Clayton approached the National Health Research and Development Program, a research-funding body in the Department of National Health and Welfare, and arranged for a representative of it to attend the next meeting of the group, on 2 December. That meeting was chaired by Dr Frances Shepherd, an oncologist at the Toronto General Hospital. Other participants included Dr Clayton, Dr Davey, Dr Naylor, Dr Roslyn Herst (the deputy medical director of the Toronto blood centre and the chair of the medical and scientific advisory council of the Ontario chapter of the Canadian Hemophilia Society), Mr Gregory Smith of the National Health Research and Development Program, and several Ontario public health officials and academics. Dr Shepherd told the group that the number of hemophiliacs diagnosed with AIDS in the United States had climbed to nine. If AIDS proved to be transmissible through blood products, she said, "it would have serious and far-reaching implications with respect to the donation and distribution of blood and blood products." The meeting discussed a U.S. study suggesting that cryoprecipitate was safer than factor concentrates. Although the Laboratory Centre for Disease Control was about to publish the preliminary results of a continuing study of immune deficiency among hemophiliacs in Montreal, no reference was made to those results.

During the meeting on 2 December, it was proposed that a study be conducted involving 200 homosexual men and fifty to 100 hemophiliacs. It would, among other things, document the prevalence of immunologic abnormalities and the incidence of AIDS in hemophiliacs. Recommendations then would be made for handling blood from affected individuals and on cost-effective screening programs for high-risk populations. A modified version of the proposal, involving only homosexual men, was supported by the Ontario Ministry of Health. The component of the study involving hemophiliacs was not carried out because difficulties were encountered in assembling a group of subjects large enough to produce statistically significant results.

The only study of immune abnormalities in hemophiliacs conducted in Canada before 1983 was the Montreal study mentioned earlier, conducted by Dr Christos Tsoukas in collaboration with Dr Strawczynski and two senior colleagues at the Montreal General Hospital, Dr Phil Gold and Dr Joseph Shuster. It began in the autumn of 1982, and followed the medical histories of thirty-two severe hemophiliacs, all of whom used more than 40,000 units of factor VIII concentrate a year. The preliminary results, published in the *Canada Diseases Weekly Report* of 11 December 1982, were consistent with those of similar studies in the United States. The researchers found that "a substantial proportion" of the "asymptomatic patients with hemophilia A

may have immune dysfunction similar to that described in other population groups with AIDS and thus may be at risk for the development of severe opportunistic infections and malignancies." Dr Tsoukas and his associates concluded:

Hemophilic patients are at risk to acquire blood borne infections as a result of the frequent use of pooled blood products. Viral hepatitis has heretofore been the major transmissible agent to affect these patients. It is reasonable to postulate that an as yet undefined transmissible agent in the factor VIII preparations is responsible for the observed immune abnormalities.

As a result, they said, hemophiliacs "may therefore be at high risk for development of the full blown AIDS syndrome."

Dr Shuster, one of the co-investigators, was interviewed by the *Medical Post*, a widely distributed Canadian weekly newspaper, soon after the preliminary results were published. His comments, published in the issue of 28 December 1982, generated considerable controversy. He was reported as saying that AIDS might be caused by an infectious, blood-borne pathogen, that hemophiliacs were "particularly at risk" of contracting AIDS, and that blood donations should "be restricted until the agent responsible for the syndrome is found." He was also quoted as saying that "there is 'no question' that gay men should not donate blood until the issue is resolved." Dr Strawczynski wrote in mid-January 1983, to another physician who was treating hemophiliacs, that Dr Shuster had been "misquoted" and that the "research team" was angered by the article. Dr Tsoukas testified, however, that he shared Dr Shuster's views at that time. On 6 January 1983, Dr Martin Inwood, the director of the southwestern Ontario hemophilia program, wrote to Dr Strawczynski and Dr Herst in response to the article in the *Medical Post*. He called upon the Canadian Hemophilia Society to make a "specific policy statement that can be distributed through the organization" about the wisdom of testing for cellular measures of immune deficiency and about the safety of the plasma sources used to make blood products. A specific policy statement about testing for immune deficiency was not made. In March 1983, the Canadian Hemophilia Society's medical and scientific advisory committee did make a statement, described elsewhere in this Report, about the safety of plasma sources.

After the preliminary results of the Montreal study were published, the possibility of similar studies in Hamilton, London, Saskatoon, and Calgary was discussed. None was implemented. A national three-year study of hemophiliacs began under Dr Tsoukas's direction in August 1984.

Measures to Reduce the Risk of Contamination

The therapeutic use of blood has never been without risk. Viruses, bacteria, and other transmissible organisms have always represented a threat to those receiving blood transfusions. In response to these risks, the Canadian Red Cross Society (Red Cross) has used a variety of measures to protect the blood supply, beginning many years before the emergence of AIDS in the 1980s. The risks of spoilage and bacterial contamination were lessened by careful handling and storage. The risk of contamination from known disease-causing organisms such as those causing syphilis and, later, hepatitis B was lessened by testing every donation for their presence. Donors were questioned, or "screened," to identify those who were not in good health, from causes as simple as a cold or influenza to more serious conditions; the screening also identified those who were at greater than normal risk of being in poor health, perhaps because they had travelled to areas where transmissible diseases were endemic. Such persons might be deferred from donating, not because it was proved that they would transmit an infectious agent through their blood, but because there was an identifiable risk that they might do so.

By 1982, AIDS had emerged as a new risk to the blood supply. AIDS had a long latency period, then believed to be many months, and a high rate of mortality. Of all the cases known at the time, approximately 40 per cent were fatal. Although other theories existed, the predominant view was that AIDS was caused by an infectious agent, and throughout 1982 evidence mounted that linked the transmission of AIDS to, among other things, blood and blood products. In July 1982, the Centers for Disease Control in Atlanta, Georgia, reported the cases of three persons with type A hemophilia who had contracted AIDS, possibly through blood products. In August 1982 *Science*, a leading U.S. journal of scientific research, published an article that concluded that "[a]lthough other explanations have not been ruled out, most investigators currently think that the disease is caused by an infectious agent, possibly a new virus or a new variant of an existing virus. The spread of AIDS resembles that of hepatitis B virus." On 13 September, the Centers for Disease Control reported in its *Morbidity and Mortality Weekly Report* that "[t]he epidemiology of AIDS suggests an unidentified and uncharacterized blood-borne agent as a possible cause of the underlying immunologic defect." By

December 1982 there was mounting and persuasive evidence that AIDS was transmissible through blood components or blood products, such as factor concentrates, and by early 1983 it was apparent that measures were needed to reduce the risk that AIDS presented to the blood supply.

It would not be until April 1984 that the human immunodeficiency virus (HIV) was widely understood to be the cause of AIDS. It was not until late 1985 that a test would be implemented throughout Canada that determined whether blood donations contained that virus by testing for its antibody. Until that time, several less precise measures were available to reduce the risk of transfusion-associated AIDS.

This chapter describes the response of the Red Cross to the risk of transfusion-associated AIDS in Canada, from the time the risk became apparent in 1982 to the time of and beyond the implementation of testing for HIV antibody in the autumn of 1985. The implementation of testing is described in the next chapter.

Donor recruitment, pre-AIDS

In the 1980s, the Red Cross blood transfusion service was a professional organization operated by a national office that directed the activities of seventeen local blood centres. The most senior person in the blood transfusion service was the national director, Dr Roger Perrault, who reported directly to the secretary general of the society. The most senior officials at the national office and at the local centres were physicians who reported to the assistant national director, Dr Martin Davey, who in turn reported to Dr Perrault. Dr Perrault, an eminent and highly qualified transfusion expert, had assumed the position of national director of the blood transfusion service in 1974. He had inherited a service that was in serious need of modernization. Dr Perrault had reformed the service by hiring medical directors for the local centres and by striving for standardization of procedures for the centres to follow. This inevitably involved an effort to limit the discretion that local centres had to depart from national standards.

There was one important aspect of the blood program that the national office and the national director of the blood transfusion service did not control. The blood donor recruitment program was not part of the blood transfusion service, but was one of a collection of regional programs grouped together as "field services." These included, among other services, the home care program, domestic relief, and a water safety program.

The blood transfusion service and the blood donor recruitment program were managed through separate administrative structures, each with its own national director who reported to the secretary general. The two administrative structures were quite different. The structure of the blood transfusion service was centralized and hierarchical, managed by a national office to which the local centres reported. The responsibility for blood donor recruitment

was exercised at the local level and was divided among the ten provincial divisions of the Red Cross, with personnel supervised by divisional commissioners. Until 1987, the secretary general had only limited authority over the commissioners and then only in matters related to national policy. In other matters, the commissioners were accountable to divisional governing bodies. Coordination of blood donor recruitment among the divisions was effected through a national coordinator, on the staff of the national office, and a national advisory committee on blood donor recruitment, which consisted of the chairs of each of the divisions and the national chair. That committee was distinct from the blood transfusion service advisory committee.

Eighty per cent of the cost of the blood donor recruitment program was paid for by the provincial governments and the remainder by the Red Cross. The Red Cross chose to pay for 20 per cent because it thought its financial contribution would attract volunteers and assist its charitable fundraising. The blood donor recruitment program relied upon a large number of volunteers who performed such tasks as telephoning donors to ask them to donate again and greeting them at clinic sites.

The Red Cross collected blood at a few fixed donor clinics and at many more mobile clinics. The mobile clinics were often held in churches, schools, legion halls, factories, offices, and similar sites in both urban and rural areas. They could be more expensive than fixed clinics, particularly in remote communities, because of the additional costs of transportation and staff time. The mobile clinics provided an important link between the Red Cross and smaller communities, not only by attracting more donors but also by giving the residents, who would probably not go to the permanent clinics in major centres, the opportunity to donate blood.

The blood donor recruitment program of the Red Cross was responsible for selecting the location of mobile blood clinics, for recruiting the donors, for greeting and registering the donors, and for caring for the donors after the donation. The responsibilities of the blood transfusion service in the donation process began at the technician's table before the donation took place and ended when the donor left the donation couch.

Before the emergence of AIDS, the Red Cross blood donor system was designed to obtain donations from a large number of persons quickly. One important strategy in recruiting was that of "donor challenges," in which corporations or departments of corporations were pitted against one another to see which could supply the greater number of donors. Similar recruiting methods were used in schools and universities. The challenges succeeded in encouraging donation through friendly competition, but they created a risk that donors were volunteering not from altruism but as a result of peer pressure. Peer pressure could make it difficult for persons to withdraw from the donation process as a result of questions asked during the screening process, particularly in mobile clinics where there was little, if any, privacy. Mobile

clinics rarely had separate areas where donors could speak in confidence with a nurse. The screening, and donation, took place in the presence of other donors. Before the emergence of AIDS, this was not a serious problem.

Nature of donor questioning and examination in 1982

Before the emergence of AIDS, it was recognized that one of the principal means of protecting the safety of the blood supply was by the careful selection of donors. Experience had proved that volunteer donors, who gave their blood for altruistic reasons, were inherently safer than paid donors who had a financial motive for giving blood even if they were not healthy enough to do so. It was accepted that screening donors at the time of donation, according to established criteria, was an effective and necessary means both of protecting recipients from blood that might carry infectious agents and of protecting donors who might otherwise be adversely affected by giving blood.

A prospective donor who entered a Red Cross blood clinic in 1982 was not given a physical examination. A volunteer registrar gave the donor a written questionnaire that read as follows:

Please read this sheet and notify the Clinic Technician if your answer is "YES" to any of the following questions. [After filling out the questionnaire, donors routinely met the technician, a Red Cross employee, for a test of hemoglobin level and blood type.]

A yes answer does not necessarily disqualify you as a blood donor.

A further discussion with our Clinic Nurse is required to determine eligibility.

1. Do you participate in any other blood programme?
(plasmapheresis, cell pheresis, etc.).
2. Have you ever fainted at any previous donation?
3. Do you now or have you ever had:
Hepatitis or "yellow jaundice", Epilepsy (Seizures)
High blood pressure, Lung Disease, Cancer, Malaria, Diabetes,
Kidney Disease, Heart Disease, Blood Disease
Any other chronic health problem?
4. In the past 3 years:
Have you been outside Continental North America?
Did you take medication to prevent Malaria?
5. In the past six months have you had:
Any serious illness or have you required physician or hospital care?
Transfusion of blood or blood products, Vaccination, Tattoo, Ear
piercing, Acupuncture?
Contact with Infectious Hepatitis?
Have you been pregnant? Did you breast feed your infant?

6. Do you now have:

Any active allergic condition (Asthma or Hay Fever), sore throat, cold, flu, skin problems?

7. Are you presently taking any medications or injections?

8. Within the last 24 hours:

Have you taken aspirin or anything for headache, cough, cold, arthritis or stomach upset? [Emphasis in original.]

The donor was expected to tell the technician if he or she had answered yes to any of the questions. If the donor had, he or she would then be interviewed by the clinic nurse, who would determine whether that person should be deferred permanently or temporarily from donating. The nurse would be guided by the "donor criteria manual," an internal Red Cross document prepared by a committee of medical directors that set out standards for deferring donors. In addition to such factors as age, weight, and frequency of donation, the manual listed the conditions that gave rise to temporary deferral, such as chicken-pox, meningitis, and the therapeutic use of certain drugs. The manual also listed the conditions that would result in rejection (permanent deferral) of blood donors, such as cancer or intravenous drug addiction. The Red Cross donor criteria manual had been revised in 1979. In 1982, it contained no mention of AIDS, its associated symptoms, or the groups of persons at high risk of contracting AIDS.

The standards for accepting or rejecting donors were prescribed by the national office, and were not to be altered without its approval or direction. They could not, and did not, cover every possible circumstance, however. Some clinical discretion therefore could be exercised at the local level by nurses at the blood clinics and by medical directors who, although rarely in attendance, could be consulted by the nurses.

Recruitment pressures

The supply of blood components is limited in Canada by the number of blood donors in the adult population. Historically, only about 4.5 per cent of the adult population has donated blood. The Red Cross, on the other hand, has no control over the demand of blood by hospitals. During the 1970s there was considerable growth in the demand for blood and blood components as a result of new surgical procedures, such as organ transplants, that required large amounts of blood. The Red Cross could not refuse to supply a blood component or blood product even if the local medical director believed that it was not going to be used appropriately; it could only advise physicians against inappropriate use. There were two reasons for this restriction. First, the Red Cross functioned on a "demand" basis. There were no contracts specifying the number of units of blood, blood components, or blood products that it would deliver to any hospital. It was required to fulfil all requests. Second,

although the medical directors were physicians, they were not the physicians treating the patients who needed the blood components or products.

Beginning in 1978, the Red Cross began to experience continual blood shortages, particularly in Toronto, Montreal, and Vancouver. Demand was rising, and the resources to recruit donors were limited.

One might have expected that a principal advantage of a national blood system was an ability to transfer blood and components from areas of surplus to areas of shortage. In practice, however, although some interprovincial transfers did occur, they were generally not encouraged. During the mid-1980s, the shortages in Toronto, Montreal, and Vancouver became increasingly serious. Surpluses from Newfoundland were often flown in to relieve the shortages in those cities, and in return the St John's blood centre imposed a levy to cover its costs. On one occasion Dr Richard Huntsman, the medical director of the St John's blood centre, proposed that this be made a regular procedure so that the centre could schedule out-of-province shipments and plan its collections accordingly. This would have had the additional benefit for Newfoundland of defraying the cost of surgery performed on its residents, who were regularly sent to Halifax or Toronto for major procedures. The national office would not permit a permanent schedule of transfers.

December 1982: Growing recognition that AIDS was transmissible by blood

By the beginning of December 1982, it was clear that the AIDS epidemic was spreading at an alarming rate. In the United States, some 800 cases had been reported. The United States was the epicentre of the reported epidemic, but of those cases that had been reported in other countries, approximately 40 per cent (21 cases) were in Canada. Nine of the persons diagnosed in the United States with AIDS were hemophiliacs. Investigators at the Centers for Disease Control were becoming convinced that the agent responsible for the development of AIDS could be transmitted through blood products administered intravenously. A limited study in Wisconsin had revealed that hemophiliacs treated with factor VIII concentrate had reduced cellular immunity, a characteristic of reported AIDS cases, whereas hemophiliacs who had been treated only with cryoprecipitate had normal cellular immunity.

These facts were reported at a meeting in Toronto on 2 December 1982 of the ad hoc AIDS group. This was a multidisciplinary group that had been formed in August after discussions between the Red Cross and the Bureau of Biologics, the federal body regulating the blood supply, about the need for research. The meeting was chaired by Dr Frances Shepherd, a hematologist at the Toronto General Hospital. Representing the Red Cross were Dr Martin Davey, the assistant national director of the blood transfusion service, Dr Derek Naylor, the director of blood products services, and Dr Roslyn Herst, the deputy medical director of the Toronto blood centre. Also in attendance were Dr Alastair Clayton, the director general of the Laboratory Centre

for Disease Control (the federal body responsible for surveillance of disease), several epidemiologists from the University of Toronto and the Ontario Ministry of Health, and other medical researchers and government officials. In the briefing paper prepared for the meeting, Dr Shepherd wrote:

The epidemic nature of this disease, now involving groups without a homosexual life style, is of great concern. The mortality is equally disturbing. Overall 21% of KS [Kaposi's sarcoma], 47% of PCP [*Pneumocystis carinii* pneumonia] and 68% of KS and PCP patients have died. However, less than 25% of patients diagnosed prior to June 1981 are still alive. The possible transmissibility by blood products is even more disturbing and has implications for the National Transfusion Service and public at large. In view of our recent identification of this problem in Toronto and the apparent increase of frequency of reporting, we think the epidemic wave is beginning here as well.

The members of the group resolved to prepare and submit a grant application for a study to determine the clinical epidemiology of AIDS.

Over the next few months, several important meetings were held in the United States at which significant evidence was presented that AIDS was transmissible by blood or blood components. A fuller discussion of these meetings and other events in the United States is discussed elsewhere in the Report.

The first of these events was a meeting of the blood products advisory committee of the U.S. Food and Drug Administration on 3 and 4 December 1982, described in Chapters 9 and 27, at which Dr Bruce Evatt of the Centers for Disease Control reported that AIDS was spreading at an almost exponential rate in an epidemiologic pattern that seemed to be similar to that of hepatitis B. He said that eight hemophiliacs receiving factor concentrates had been reported with AIDS, and about five additional cases had been reported following blood transfusions – one of them a child who had received an exchange transfusion at birth. This meeting was widely attended by members of the U.S. blood-banking industry. Dr Lewellys Barker, the vice-president for health services of the American Red Cross, said at the meeting that, although there was as yet no proof, "it looks very much as if [AIDS] is caused by a transmissible agent." Dr Thomas Zuck, a former director of the division of blood and blood products of the Food and Drug Administration, described the meeting in his testimony at the Inquiry as a "wake-up call" and "a watershed."

After that meeting, events unfolded rapidly. On 10 December 1982, the *Morbidity and Mortality Weekly Report*, the weekly publication of the Centers for Disease Control, reported the first confirmed case of transfusion-associated AIDS, in a twenty-month-old San Francisco child. The child, who had died, had received multiple units of blood components at birth. The donor of one of the units had not developed symptoms at the time of donation but later

died of AIDS. By December 1982, the Centers for Disease Control was investigating five additional cases of AIDS that had been reported in persons who had received blood transfusions.

On the same day, 10 December, there was an informal meeting of the U.S. Food and Drug Administration and the four U.S. manufacturers of blood products: the Cutter Biological Division of Miles Laboratories Inc., Armour Pharmaceutical Company, the Hyland Therapeutics Division of Travenol Laboratories Inc., and Alpha Therapeutic Corporation. The blood product manufacturers, who obtained most of their plasma from persons who were paid for it, were asked to stop collecting plasma from such high-risk areas as New York City, San Francisco, and the Hollywood area of Los Angeles.

The American Association of Blood Banks represented a large proportion of the community and hospital blood banks in the United States, including the American Red Cross. On 17 December 1982, Dr Joseph Bove, the chair of the association's committee on transfusion-transmitted diseases, wrote to its members emphasizing the threat of AIDS to the blood supply and the need for action to address that threat:

My current best guess is that we are dealing with an infectious agent able to be spread by blood and blood products and that individuals who receive large quantities of factor concentrate are at an increased risk.

I think we are under great pressure to do "anything and everything" to curtail the spread of AIDS. Our committee needs to decide what to recommend. In our two previous problems – ALT [a surrogate test for hepatitis B infection] and Hepatitis B Vaccine – we took an essentially passive course suggesting that available information did not warrant a widespread change in current activity or policy. I, for one, do not believe that a similar stance is appropriate for AIDS.

On the same day, Alpha Therapeutic Corporation announced that it was changing the way in which it questioned and examined its donors in order to attempt to exclude persons at high risk from AIDS. It would ask them directly whether they had resided in Haiti, were intravenous drug abusers, or were homosexual men.

On 20 December, Dr Davey, the assistant national director of Canadian Red Cross blood transfusion services, and Dr John Derrick, the director of blood products services, sent an information letter about AIDS to the medical directors of the seventeen Canadian blood centres. The letter referred to the possibility that AIDS was transmissible by blood and warned that pressures would be put on the Red Cross to respond to the threat:

[C]ontinuing developments ... are considered by some U.S. authorities to be sufficiently supportive of the postulate that AIDS is a disease transmissible by blood and blood products to warrant immediate action with

respect not only to donor selection but also to the utilization of blood, blood products, and plasma derivatives, Factor VIII concentrate in particular ... Organizations such as the American Red Cross, and the Council of Community Blood Centres are considering how to approach the elimination of high risk groups from their donor panels ...

Such reactions will probably arise in Canada with the publication in the Canada Diseases Weekly Report of December 11, 1982 of a pilot study on AIDS and hemophilia A patients carried out in Montreal, and after forthcoming articles in the Medical Post and the popular press. The CRCS [Canadian Red Cross Society] response to the resulting pressures cannot be delayed by the need to search and to wait for funding implicit in the Canadian approach to the AIDS problem to date.

Their letter described actions being taken, or "under consideration," by the Red Cross:

- a. Continued provision to CRC BTS [Canadian Red Cross Society blood transfusion service] Centres of information, supplemental to this [information letter], relative to the AIDS problem in Canada, with particular reference to the possibility of transmission through transfusion of blood and blood products.
- b. A request to CRC BTS Centres to help ensure the reporting of suspected cases of AIDS to LCDC [Laboratory Centre for Disease Control] and to Provincial Health Authorities, and of cases involving blood and/or blood products to the National BTS Office.
- c. Promotion of the development of, and liaison with, clinical and laboratory investigational groups and facilities in Canada which may be of assistance in the recognition, diagnosis and investigation of AIDS cases.
- d. Consideration of support for studies that are particularly relevant to the possible involvement of blood products in the transmission of AIDS. A request for project submissions will be made to BTS Centres.

The letter went on to say that the evidence linking AIDS and blood transfusion was not sufficiently strong to warrant the taking of direct measures that would restrict persons at high risk of contracting AIDS from donating blood:

The etiology and clinical epidemiology of AIDS remain poorly defined in the U.S., and in Canada the extent of the problem is not yet known. Thus, definitive action toward excluding any group from donating blood or changing radically any aspect of transfusion practice should not be undertaken at present.

Rather, contingency planning will be carried out under the aegis of appropriate groups such as the CRC BTS Immunology-Virology Working

Group and the CRC BTS Advisory Committee and appropriate action will be taken if, and as, justified by further events and after consultation with concerned professional groups.

Dr Perrault, the national director of the blood transfusion service, explained in his testimony why the Red Cross was reluctant to take any measures to exclude donors at a high risk of contracting AIDS despite its apparent recognition that the causative agent of AIDS might be transmissible by blood. He said that the continuing blood shortages forced the Red Cross to take a "cautious approach" to measures that could result in reducing the number of blood donors.

From other sources, however, there were calls for the Red Cross to be more rigorous in its donor-screening practices. On 28 December 1982, as had been predicted in the letter from Dr Davey and Dr Derrick, the *Medical Post* published an article, entitled "Blood Bank's Hidden Bomb," that summarized findings of a study conducted by Dr Christos Tsoukas and colleagues of McGill University. The study, the first of immune functioning in hemophiliacs in Canada, found that 70 per cent of a group of hemophiliacs had abnormally low numbers of T-cells. These cells are produced by the body to combat infection and the number of them is a measure of the health of the immune system. Dr Joseph Shuster, a senior member of the research team, was quoted in the article as saying that "there is 'no question' that gay men should not donate blood until the issue is resolved." The article continued:

While it may be unconstitutional for blood donor clinics to ask about sexual preference, [Dr Shuster] suggested that an information campaign be launched urging gay men not to give blood for the time being.

While that idea has also been suggested by Red Cross officials in the U.S. and Canada, the organization has not changed its policy yet.

"We do not have any immediate plans for such action (excluding high risk groups from blood donation) because we do not have the evidence that would justify taking it," said Dr Martin Davey, assistant national director of the Canadian Red Cross Society's blood transfusion service, in Toronto.

"The hemophilia story does imply that blood or blood products, plasma proteins, might be one of the things that transmit it, and that perhaps one shouldn't use blood from the high risk population groups," he added.

"It's not very simple socially to identify these among blood donors and it could have quite adverse effects on our program of recruitment if we acted at this stage to do so when we have no evidence that doing so will actually make the syndrome go away. If, for instance, it is just exposure to a lot of other people's proteins, that may happen irrespective of who or where the proteins come from."

In the article, Dr Davey was quoted as setting out a rigorous standard of proof that would be required before persons at high risk of contracting AIDS were excluded:

"If an agent is identified, if a test can be developed for the carriers as has happened for hepatitis B, then we would have a reliable, feasible way of saying we will exclude blood from these people because we have identified them positively as having an injurious agent in their blood. We're nowhere near that stage.

"Question one is, 'Is it a transmissible agent?' Question two is, 'What type?' Then identify it, and find some means of screening for it – all of that process is still to be done, and we don't even know if question one has a positive answer."

January 1983: Adoption by U.S. blood bankers of measures to defer donors at higher risk

By the end of December 1982, the Centers for Disease Control in Atlanta believed it had strong evidence that AIDS was transmissible by a blood-borne agent. On 4 January 1983 it held a public meeting to formulate recommendations for the prevention of AIDS, with special emphasis on the possible transmission of AIDS through blood and blood products. The meeting was attended by representatives of the volunteer blood-banking industry, including the American Red Cross; representatives of the commercial blood product manufacturers; medical and scientific experts from the Centers for Disease Control, the National Institutes of Health, and the Food and Drug Administration; and representatives from hemophilia and gay organizations. There were no Canadian representatives.

There was considerable discussion at the meeting about the need to exclude from the blood supply persons at high risk of transmitting AIDS. Although there was agreement that such potential donors should be excluded, no consensus was reached as to the best method of doing so. The principal methods discussed were

1. Voluntary restriction by potential donors within high risk groups.
2. Exclusion of donors on the basis of history and/or physical examination at the time of donation, e.g., a positive response to questions such as, "Have you had sexual contact with another man?" "Are you a past or present intravenous drug user?" "Are you a Haitian?" etc. On physical exam, patients with lymphadenopathy etc. could be excluded.
3. Use of a "surrogate" laboratory test; a test which when positive is associated with high risk groups for AIDS.
4. A combination of these strategies.

The summary of the meeting described the advantages and disadvantages of the various methods:

Voluntary restriction has the advantage of enabling high risk groups to play a major and responsible role in protecting others in society. It is independent of the blood supply system. It is inexpensive, and is relatively easy to initiate. The disadvantages are that it has the limitations of not being able to influence less responsible persons and being unlikely to reach and motivate some proportion of those for whom it is intended.

Questioning donors for their nationality, sexual orientation or personal habits has the advantages of being an easy extension of the screening history already used in blood donation, is inexpensive, can be directed toward high risk groups and causes little disruption in the blood collection and processing routine. It has the disadvantage of being potentially intrusive into personal matters, may be viewed as unethical, might institutionalize a stigma on groups already prone to prejudice and persecution, and may be ineffective in identifying persons in these high risk groups. Concerns about record privacy have been raised. A considerable proportion of practising homosexual males may not consider themselves high-risk for AIDS and others may be reluctant to disclose their sexual orientation. Similarly, recently emigrated Haitians and drug users may be reluctant to identify themselves. Some commercial plasmapheresis processors are already excluding by history some AIDS high risk groups.

Surrogate laboratory tests have the advantages of being objective and can be done on specimens already being drawn for HbsAg [that is, testing for the hepatitis B surface antigen]. They respect donor privacy and may be most effective in eliminating potential transmitters of AIDS. They have the disadvantage of adding expense to the blood collection process, both through test cost, administrative overhead, and loss of blood units already collected. Further, they may stigmatize as unsatisfactory many "normal" donors for each potential AIDS transmitter that is rejected.

The surrogate laboratory tests for AIDS would not test for AIDS itself or the presence of its causative agent but rather, for example, for markers of other diseases that were frequently found in persons with AIDS or infected with the causative agent of AIDS. It was known that some persons infected with AIDS or its causative agent were or had also been infected with the hepatitis B virus. A test that could identify present or past infection with hepatitis B virus might therefore be of use in identifying persons infected or at high risk of infection with AIDS or its causative agent.

The participants at the 4 January 1983 meeting were told the results of a study by Dr Thomas Spira of the Centers for Disease Control. Dr Spira had examined samples of serum from persons known to have AIDS and from

control groups of persons at high risk to determine the efficacy of various surrogate tests. A number of the tests were found to be effective in identifying persons at high risk of contracting AIDS. These included tests for antibodies against the core, or inner part, of the hepatitis B virus that were both commercially available and easy to perform. They were considered useful as surrogates because of the high proportion of homosexual men who had at some time been infected with hepatitis. They were different from the tests used to screen blood donations for the hepatitis B virus because they detected antibodies that remained after a hepatitis B virus infection had resolved. They would not identify persons infected with AIDS or its causative agent, but would identify some of the persons who could be at high risk of such infection.

Dr Spira found that, of the known AIDS cases in which the person was homosexual, 88 per cent tested positive for the hepatitis B core antibody (anti-HBc). All twenty-one of the known persons with AIDS who were intravenous drug users tested positive, as did 87 per cent of the known persons with AIDS who were Haitian. The hepatitis B core antibody test was also found to have identified as positive from their blood samples 79 per cent of the "control" groups of homosexuals and bisexuals used in his study and 36 per cent of Haitian "controls." A second test, the hepatitis B surface antibody test, identified as positive fewer of the known AIDS cases than did the test for hepatitis B core antibody. The hepatitis B surface antibody test did, however, identify a similar proportion of the control group.

For various reasons, reflected in the summary of proceedings, the participants did not reach agreement about the best method of excluding persons at high risk of contracting AIDS. As noted:

The workgroup participants represented various organizations, governmental agencies and constituent groups concerned with and affected by AIDS and the blood and plasma donation process. They have differing perceptions of:

1. The likelihood that AIDS is caused by a transmissible agent;
2. The risk of AIDS from blood donation (both whole blood and pooled plasma); and
3. The best approach for establishing altered guidelines for blood donation, donor screening or testing and donor restriction.

The meeting concluded with a recommendation that the Centers for Disease Control, the Food and Drug Administration, and the National Institutes of Health develop joint recommendations for reducing the risk of transfusion-associated AIDS.

A number of participants at the meeting, including Dr Donald Francis of the Centers for Disease Control, submitted recommendations to the assistant director of the U.S. Department of Health and Human Services on 6 January 1983. With respect to whole blood and plasma collection, Dr Francis proposed that all blood and plasma donors be deferred if:

1. They are IV [intravenous] drug users (already in place).
2. They are sexually (heterosexual or homosexual) promiscuous (more than an average of 2 different people per month for the previous 2 years).
3. They have had sexual (heterosexual or homosexual) contact with someone who is sexually promiscuous or an IV drug user in the past 2 years.
4. They have lived in Haiti in the past 5 years.
5. They have a serologic test positive for anti-HBc.

With respect to surrogate tests Dr Francis said:

There is good evidence that this will eliminate over $\frac{3}{4}$ of AIDS "infected" donors. It will also defer about 5% of U.S. blood donors and add about \$5 to each unit of blood and plasma. These seem to be small prices for preventing a serious disease and a potentially dangerous panic.

The value of the hepatitis B core test as a surrogate for AIDS was uncertain. Although Dr Spira's data lent support to surrogate tests, other data, released soon after, were less persuasive. For example, a study of fifty-three homosexual men who had been treated in a sexually transmitted disease clinic in northern New York State found that only 37.5 per cent had one or more markers for hepatitis B.

The U.S. blood and blood products industry resisted the immediate implementation of surrogate tests because of the additional cost and the number of blood donations that would likely have to be destroyed. As an alternative, the New York Blood Center had proposed at the meeting of 4 January that a study be undertaken in New York, Los Angeles, and San Francisco to evaluate surrogate tests for cost and their impact on the blood supply.

There were two organizations representing voluntary blood banks in the United States. They were the American Association of Blood Banks, to which the American Red Cross and the great majority of hospital and community blood banks belonged, and the Council of Community Blood Centers, an association of independent community blood banks. Representatives of these organizations and of other groups, including the American Blood Commission, the National Gay Task Force, the National Hemophilia Foundation, the Centers for Disease Control, and the Food and Drug Administration, met on 6 January 1983 to attempt to develop a consensus about action to reduce the risk of transmission of AIDS through blood.

The American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers drafted and signed a joint statement that was released on 13 January. In it they acknowledged that, although the evidence that AIDS was blood borne was not "absolute," there was sufficient evidence to justify taking action, both by counselling caution with respect to the use of blood and blood products and by trying to prevent persons at high risk of transmitting AIDS from donating blood:

The finding of cases in hemophiliacs, especially those who use anti-hemophilic factor concentrate, coupled with the long incubation period and the continuing increase in reported cases, is of sufficient concern to warrant the following suggestions for action on the part of blood banks and transfusion services. We realize that there is no absolute evidence that AIDS is transmitted by blood or blood products, and we understand the difficulty in making recommendations based on insufficient data. There is a need for additional information about this disease. Public health authorities should allocate resources to study the etiology of AIDS, its mode of transmission, and appropriate preventive measures and therapy. Blood centers and transfusion services should continue to assist public health agencies investigating AIDS. Given the possibility that AIDS may be spread by transfusion we are obliged to respond with measures that seem reasonable at present. The lack of a specific test means that our major effort must revolve around two areas: 1) additional caution in the use of blood and blood products and 2) reasonable attempts to limit blood donation from individuals or groups that may have an unacceptably high risk of AIDS.

The joint statement set out the following recommendations:

1. Blood banks and transfusion services should further extend educational campaigns to physicians to balance the decision to use each blood component against the risks of transfusion, be they well-established (e.g. hepatitis, cytomegalovirus, malaria) or under investigation (e.g. AIDS).
2. Autologous blood transfusions, as an alternative to allogenic transfusion, should be considered more frequently, especially in elective surgery. [Autologous blood is the patient's own blood, deposited before surgery for use if needed.]
3. Blood banks should plan to deal with increased requests for cryoprecipitate. Altered T lymphocyte function, a component of AIDS, has been reported to be less frequent in hemophilia patients who are treated with cryoprecipitate rather than AHF [antihemophilic factor] concentrate. Although this does not necessarily imply that cryoprecipitate is free of risks, this finding may lead to an increased demand for cryoprecipitate.

4. Donor screening should include specific questions to detect possible AIDS or exposure to patients with AIDS. In particular, all donors should be asked questions designed to elicit a history of night sweats, unexplained fevers, unexpected weight loss, lymphadenopathy or Kaposi's sarcoma. All positive or suggestive answers should be evaluated before anyone donates.
5. Persons with responsibility for donor recruitment should not target their efforts toward groups that may have a high incidence of AIDS.
6. A major area of concern is whether attempts to limit voluntary blood donation by individuals from groups with a high prevalence of AIDS are appropriate at present. This question has medical, ethical and legal implications.
 - a. The presently available medical and scientific evidence that AIDS can be spread by blood components remains incomplete. Fewer than 10 cases of AIDS with possible linkage to transfusion have been seen despite approximately 10 million transfusions per year. Ongoing epidemiologic studies of all cases of AIDS are being conducted at this time. Should evidence of a clearly implicated donor population become apparent, specific recommendations to the blood banking community will be made promptly.
 - b. There is currently considerable pressure on the blood banking community to restrict blood donation by gay males. Direct or indirect questions about a donor's sexual preference are inappropriate. Such an invasion of privacy can be justified only if it demonstrates clear-cut benefit. In fact, there is reason to believe that such questions, no matter how well-intentioned, are ineffective in eliminating those donors who may carry AIDS. Blood banks should work with the leadership of groups which include some individuals at high risk of AIDS.
7. While there is no specific test for AIDS, there are laboratory and clinical findings that are present in nearly all AIDS patients. The use of these non-specific markers, for example, lymphopenia, immune complexes, and anti-HBc, are being evaluated in those areas of the country where AIDS is prevalent. We do not advise routine implementation of any laboratory screening program for AIDS by blood banks at this time.

The statement, which recommended neither surrogate tests nor direct questioning of donors about high-risk behaviour, was a disappointment to persons who had hoped for strong measures to reduce the risk of contamination of the blood supply. Dr Francis testified that the joint statement was "an extremely confusing document" that minimized the real issue of blood-borne transmission and the urgency of dealing with it. He testified that the refusal to question donors about whether they engaged in behaviour that placed them at risk of contracting AIDS or were part of a group at high risk of contracting

AIDS made no epidemiological sense, considering that 75 per cent of the cases of AIDS were found in homosexual men and another 12 to 15 per cent in intravenous drug abusers. Questions about symptoms, which were advocated in the joint statement, were useful but not nearly as important as questions about risk. He said that, in the course of assisting in the development of the hepatitis B vaccine, he had interviewed many homosexual men, in great detail, about their sexual practices. It was his experience that, as long as the questions were asked in private and in a non-judgmental way, they did not cause offence and were answered with candour.

The Canadian Red Cross received a copy of the joint statement within days of its release. Discussion of it within the society, described in the following pages, began soon thereafter.

On 14 January 1983, the day after the release of the joint statement, the U.S. National Hemophilia Foundation met in New York and recommended steps to minimize the risk of exposure to AIDS in the treatment of hemophiliacs. The recommendations, aimed at manufacturers of factor VIII concentrate, urged more stringent efforts than those proposed in the joint statement, including the direct questioning of donors about whether they were members of groups at high risk of contracting AIDS:

Serious efforts should be made to exclude donors that might transmit AIDS. These should include:

1. Identification, by direct questioning, [of] individuals who belong to groups at high risk of transmitting AIDS, specifically male homosexuals; intravenous drug users; and those who have recently resided in Haiti.
2. Evaluation and implementation (if verified) of surrogate laboratory tests that would identify individuals at high risk of AIDS transmission.
3. In addition, the manufacturers should cease using plasma obtained from donor centers that draw from population groups in which there is a significant AIDS incidence. It is clear from the epidemiologic data that the pool of individuals at risk for AIDS transmission is not uniform throughout the country and that a great deal could be achieved by excluding donors from the "hot spots."

January–February 1983: Consideration of donor deferral in Canada

Dr Derrick, whose title was now "Advisor, Regulatory Affairs and Good Manufacturing Practice" of the Canadian Red Cross, attended the U.S. National Hemophilia Foundation meeting and reported its results – in particular, the efforts being undertaken by the U.S. voluntary blood sector as described in the joint statement – to his colleagues at the Red Cross. He emphasized that the American Red Cross and the New York Blood Center had both said that it was incumbent on them to try to find effective methods to exclude

high-risk donors, but opposed the direct questioning of volunteer donors about their sexual preferences or activities and about intravenous drug use. They also opposed the closing of blood clinics in high-risk areas. Dr Derrick suggested that the Canadian Red Cross donor questionnaire could be used as a means of "giving high-risk donors the opportunity to exclude themselves without embarrassment," if, presumably, it was revised.

On 17 January 1983, Dr Perrault sent a fact sheet about AIDS to the Red Cross's provincial divisions, which were responsible for donor recruitment, to help them in dealing with questions from the media about the disease. He suggested that such questions should preferably be dealt with by local medical directors. The fact sheet said that "no change in current practices" was then contemplated. On the same day, Dr Perrault wrote to the society's secretary general – its chief executive officer – that

[t]he issue is well in hand as far as the technical aspects are concerned. The only difficulty is that we are dealing with a situation that is evolving very rapidly but still without a definite cause for this "new disease." I have discussed the matter last Friday with my colleague at the American Red Cross, Dr. Lew Barker, and he has assured me that any new development in their area would be communicated to us immediately.

The Red Cross had extensive experience in dealing with the media, but its blood transfusion service – before the emergence of AIDS – had had little experience in dealing publicly with politically sensitive issues. The Red Cross's public relations activities were handled independently of the blood transfusion service, both at the national level, where public relations reading material was prepared, and at the divisional level, where it was distributed. The blood transfusion service had no separate public relations department or budget for preparing materials such as pamphlets to be distributed to donors. All reading material for donors was prepared under the blood donor recruitment program, which had a budget for that purpose. The additional public relations responsibilities that devolved to the blood transfusion service in response to AIDS were not accompanied by an increase in its budget.

By mid-January 1983, the Canadian Red Cross had also learned of the results of the direct questioning that Alpha Therapeutic Corporation had been conducting of persons from whom it bought plasma. Of six to seven thousand donors who had been questioned during approximately three weeks about high-risk behaviour, 308 had been excluded because of their answers and an even larger number of persons excluded themselves without stating a reason.

On 21 January 1983, a meeting was held of the immunology-virology working group of the Red Cross blood transfusion service. This was a committee of scientists from within and without the Red Cross. Dr Davey and Dr Derrick represented the national office of the blood transfusion service, and the membership included a number of local medical directors and deputy

medical directors. Among those attending on this occasion was Dr Roger Dodd, the head of the transmissible diseases and immunology laboratory of the American Red Cross. Dr Derrick reviewed the issue of a link between AIDS and blood transfusion, stressing "the lack of conclusive evidence" that AIDS was transmissible via blood products.

Dr Derrick and others in the Red Cross defined "conclusive evidence" by a strict standard – fulfilment of Koch's postulates. Dr Robert Koch, a nineteenth-century pioneer in bacteriology, had defined a standard for proving that an infectious agent caused a particular disease. To fulfil it, one would isolate the agent suspected of causing the condition in one person or animal and inject it into another person or animal, determine whether the same condition developed, and, if it did, isolate the agent from the recipient. When Dr Derrick referred to "conclusive evidence," he was, according to Dr Perrault and Dr Davey, subscribing to the "full rigour" of Koch's postulates.

Although acknowledging "the lack of conclusive evidence," Dr Dodd pointed out that "the view that AIDS could be transmitted in blood transfusion was quite widely held." The minutes of the meeting record that he went on to say that

the inclusion in the donor screening procedure of direct questioning with reference to whether or not the donor might fall in a high risk category had not been adopted by the volunteer blood donor agencies in the U.S. However, he could see that the Canadian system of donor screening lent itself to the inclusion of pertinent questions which could be at least partially effective in excluding high risk donors without alienation effects.

Presumably, Dr Dodd was referring to the Canadian Red Cross donor-screening questionnaire, which could readily have been revised to include questions that would detect symptoms of AIDS or membership in a high-risk group. The Red Cross did not accept direct questioning about membership in a risk group, however, because it was concerned that it might offend donors. This concern was not the result of any study of donor attitudes by the Red Cross.

Instead, the Red Cross proposed that, if at some time in the future the evidence linking AIDS to blood transfusion became sufficiently conclusive to justify rejecting blood donations from persons in high-risk groups, the most acceptable method of preventing those persons from donating would be to communicate with representatives of high-risk groups and spread the message through them. The members of the immunology-virology working group agreed with that position.

The working group also reviewed and endorsed the joint statement of the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers. This included a recommendation that donors be questioned specifically about the symptoms of AIDS. Dr Davey

said that donor criteria would be reviewed by a representative group of local medical directors.

On 24 January, Dr Davey sent a copy of the U.S. joint statement to the medical directors. He told them that it had been endorsed by the immunology-virology working group and that it was proposed that the blood transfusion service adopt the statement as "working policy" for the Canadian Red Cross. He asked all medical directors to notify him of their agreement or disagreement by 4 February 1983. The medical directors adopted the joint statement unanimously.

In the United States, also on 24 January, the committee on transfusion-transmitted diseases of the American Association of Blood Banks learned of another suspected case of transfusion-associated AIDS, a child who had been admitted to a Texas hospital. The child had received transfusions from seven donors, one of whom had AIDS. Dr Joseph Bove, the committee's chair, said:

There is little doubt in my mind that additional transfusion related cases and additional cases in patients with hemophilia will surface. Should this happen, we will be obliged to review our current stance and probably to move in the same direction as the commercial fractionators. By that I mean it will be essential for us to take some active steps to screen out donor populations who are at high risk of AIDS. For practical purposes this means gay males.

On 26 January 1983, the American Red Cross amended its donor-screening practices. Its centres were told to expand their questioning of potential donors "to include specific questions to detect potential donors with symptoms of possible AIDS or histories of exposures to persons with AIDS." The centres were told not to ask questions about a donor's sexual preference or to ask a donor to withdraw voluntarily from giving blood. The American Red Cross also provided its centres with an information package which included a list of gay community organizations and publications; recommendations from the U.S. National Hemophilia Foundation for the treatment of hemophilia; and a letter that could be sent to physicians about the transmission of AIDS through blood and blood products. In that letter, physicians were advised to increase the use of the patient's own previously deposited blood:

While the likelihood that transfusion of a blood product plays any significant role in the epidemiology of AIDS is small, this possible added risk factor in blood transfusion should be considered when ordering blood for a patient. Autologous blood transfusions should be considered more frequently, especially in elective surgery. Because American Red Cross Blood Services is determined that the products distributed by its regional blood centers be the safest blood available, we are now asking prospective donors questions that will elicit possible symptoms of AIDS.

Two days later, on 28 January, the American Blood Resources Association, which represented the U.S. commercial plasma fractionation industry, recommended that information be given to persons at high risk of contracting AIDS to discourage them from selling their plasma. It recommended that persons wanting to sell their plasma be required to read the information documents and acknowledge that they were not members of a high-risk group.

In Canada, representatives of the Canadian Hemophilia Society and the Red Cross blood transfusion service met on 7 February 1983. The meeting produced five recommendations for the treatment of hemophiliacs: that persons who were newly diagnosed with type A hemophilia be treated with cryoprecipitate, that children who were already receiving cryoprecipitate continue to do so, that Canadian patients be treated with factor VIII concentrate that was produced from Canadian plasma, that mild or moderate hemophiliacs be treated with the synthetic analogue of a human hormone to increase the level of factor VIII in circulation, and that elective surgery be reviewed carefully to determine whether it was necessary. It also recommended that a "serious effort" be made to exclude blood donors who might be at high risk of transmitting AIDS and suggested two methods by which this might be accomplished:

- a. to expand on the CRC BTS [Canadian Red Cross Society blood transfusion service] voluntary blood donor questionnaire by the inclusion of questions more specifically related to the symptomatology of AIDS;
- b. to introduce an educational programme designed toward self exclusion by high risk group blood donors.

The Red Cross said that it agreed with the recommendation to exclude high-risk donors by modifying the donor-screening questionnaire and that

Currently CRC BTS medical directors are being canvassed as to the acceptability of donor screening criteria as outlined in the joint statement issued by the U.S. voluntary blood donor agencies and, on approval, these will be incorporated in the screening of donors.

On 8 February, the Irwin Memorial Blood Bank in San Francisco announced that it had amended its donor selection process. Donors were given information that identified the groups at high risk for AIDS. They were then asked:

To assist in deferral of prospective donors who may be at high risk for AIDS, please indicate whether any of these conditions apply to or have applied to you by answering yes or no below:

- Multiple sex partners from one of the high risk groups listed above
- Residing in Haiti

- Recurring fever over a long period of time
- Heavy night sweats
- Unexpected weight loss of 10 lbs. or more in a short time
- Enlargement of glands throughout body
- Kaposi's Sarcoma
- Intimate contact with an AIDS patient.

A "yes" response will result in indefinite deferral of the donor unless otherwise approved by an Irwin physician.

In New York City, the persons who drew blood at the New York Blood Center were told to examine donors for symptoms of AIDS and for evidence of intravenous drug use.

On 10 February, Dr Davey wrote to the Red Cross medical directors, reporting their unanimous endorsement of the U.S. joint statement that recommended asking potential donors whether they had symptoms of AIDS. He also reported that the Canadian Hemophilia Society had made suggestions about donor screening which would be reviewed by several internal Red Cross committees and then presented to a meeting of medical directors on 24 March. He said that the national office of the blood transfusion service would develop strategies for "approaches" to high-risk groups, which would also be discussed with the medical directors. He explained that autologous transfusion, which had been endorsed in the U.S. joint statement, would "not be emphasized, because of logistic problems noted by some Centres."

Dr Davey intended that his memorandum should be understood as a direction to the centres, and that they were not permitted to take any action with regard to donor screening until instructed to do so.

March 1983: Enhanced donor-screening measures in U.S. blood banks

On 4 March 1983, the U.S. Department of Health and Human Services, which included the Centers for Disease Control and the Food and Drug Administration, recommended that members of high-risk groups refrain from donating blood and plasma and that prospective donors be informed of this recommendation. It was implicit in this recommendation that a public information campaign take place and that the message be made available at blood clinics. High-risk groups were defined as

patients diagnosed with AIDS; sexual partners of AIDS patients; persons with symptoms and signs suggestive of AIDS; sexually active homosexual or bisexual men with multiple partners; Haitian entrants to the U.S.; present or past abusers of intravenous drugs; and sexual partners of individuals at high risk for AIDS.

The U.S. department also recommended an evaluation of the effectiveness of laboratory tests and of different screening procedures, such as careful questioning and physical examination of donors, in identifying and excluding blood and plasma that had a high probability of transmitting AIDS. At the time the only tests available were surrogate tests. In addition, the department recommended that physicians adhere strictly to medical indications for transfusions and encourage autologous transfusions.

Within days, volunteer blood banks in the United States took steps to inform all donors that certain groups were at high risk of contracting AIDS and that members of those groups should refrain from giving blood. The American Red Cross and the American Association of Blood Banks produced pamphlets, differing in content but both entitled *An Important Message to All Blood Donors*. Persons at high risk who were asked to refrain from donating blood included "sexually active homosexual or bisexual men with multiple partners." The volunteer blood banks also took steps to ensure that the pamphlets were read. The pamphlet produced by the American Association of Blood Banks included a "donor acknowledgment" that donors were required to sign. It said:

I have read the literature provided by the blood bank concerning Acquired Immune Deficiency Syndrome (AIDS), and understand that members of high risk groups have been asked to refrain from donating blood.

The American Red Cross did not ask donors to sign such a statement but its nurses, in the course of interviewing donors about their health history, asked whether the donors had read and understood the pamphlet.

The New York Blood Center went further than most other blood banks. On 8 March 1983, it began a program known as "confidential unit exclusion." Every donor was given a questionnaire that first described AIDS and the high-risk groups, and then stated:

We are studying laboratory methods to detect blood donations from people with greater exposure to AIDS. If you think that there is any possibility that you have had greater exposure to AIDS, as described above, we will use your blood for laboratory services only. If not, we will use it for transfusions.

The donor was then asked to check a box to express his or her wish, either that the donation be used only for studies or that it be used for transfusion. The questionnaire was to be filled out in private and it was to be folded and stapled to ensure confidentiality.

March 1983: Announcement of voluntary self-exclusion in Canada

The announcement by the U.S. Department of Health and Human Services and the measures taken by blood bankers in that country received considerable media attention in Canada. Some media reports erroneously implied that it was Canadian Red Cross policy to question donors actively about risk factors and exclude all homosexuals from donating blood. The Red Cross recognized that it was facing a difficult public relations problem. In response, an ad hoc meeting of senior personnel was held at the national office on 10 March 1983. In attendance were Dr Perrault, Dr Davey, Dr Derrick, a senior person from the blood donor recruitment service, and several members of the public relations department. They decided that the Red Cross would promote a policy of voluntary self-exclusion: the voluntary withdrawal of those at high risk, as opposed to active exclusion of members of high-risk groups. In particular it would inform persons at high risk of contracting AIDS, through their community leaders, that they should not donate blood. The meeting also decided that the donor questionnaire would include only questions about health, including questions about the signs and symptoms of AIDS, and none about membership in risk groups. The meeting effectively brought to an end consultation with the local medical directors, who had been told they would consider the issue of donor screening at a meeting on 24 March 1983.

After the meeting on 10 March, the Red Cross issued a press release which said that persons at high risk of contracting AIDS were asked not to donate blood:

The Canadian Red Cross Society advises members of groups identified as high risk of carrying Acquired Immunodeficiency Syndrome (AIDS) not to give blood.

These groups are: Patients diagnosed with AIDS, sexual partners of AIDS patients, persons with AIDS symptoms, sexually-active homosexual or bisexual men with multiple partners, recent Haitian immigrants, current or past drug abusers, and sexual partners of individuals at high risk for AIDS.

Although to date there is no conclusive evidence that AIDS is transmitted through the blood or blood products, and no cases of AIDS in Canada can be linked to blood transfusion, the Canadian Red Cross Society is doing everything possible under current conditions of knowledge to protect recipients of blood and blood products from any possible threat to their health.

The Red Cross is not considering questioning potential donors at blood clinics concerning their sexual preference or their racial origins.

The society is, however, asking members of the groups at high risk of developing AIDS to voluntarily exclude themselves from giving blood. All blood donors in Canada are voluntary donors and, as such, represent a group with a highly-developed sense of responsibility to their community. The Red Cross is confident, therefore, that donors finding themselves within the identified risk groups will exercise that sense of responsibility and will refrain from giving blood until such time as the cause and transmission of AIDS can be clarified.

The press release promised that additional steps would be taken to protect the blood supply.

Further steps which will be taken by the Red Cross to protect blood recipients from the possible transmission of AIDS through blood are:

- Expansion of the current screening process for blood donors to include specific questions to detect potential donors with symptoms of AIDS or who might be carriers of AIDS. These will be introduced as an additional safeguard despite the fact that present screening procedures are considered adequate to protect the health of donors and blood recipients.
- Participation in a scientific group devising a proposal for a large-scale study designed to determine how AIDS is transmitted.
- Evaluation of suitable laboratory tests for AIDS which may become available, with the intention of implementing them as screening measures as soon as possible.

The Canadian Red Cross Society will continue to monitor new developments, in association with other agencies in Canada and the United States, and will revise its position promptly should medical or other scientific findings indicate that a different course of action is warranted.

To ensure dissemination in the francophone media, the national press release was followed a few days later by a press conference with Dr Raymond Guévin, the medical director of the Montreal blood centre.

The Red Cross depended on "voluntary self-exclusion" to reduce the risk of contamination of the blood supply by the causative agent of AIDS. It had rejected a policy of actively deferring persons at high risk of contracting AIDS, either by asking them whether they belonged to high-risk groups or by asking them whether they had symptoms of AIDS. Under a policy of voluntary self-exclusion, persons at high risk were to be informed that they were at high risk and asked to refrain voluntarily from giving blood. For this policy to be successful, the high-risk donors had to be adequately informed. The risk groups that were described in the press release were not well defined, however. "Sexually-active homosexual or bisexual men with multiple partners" could refer to men who had had sex with two partners or 200. "Drug abusers" could refer to everyone from heroin addicts to casual users of marijuana.

Much of the reporting in the media, moreover, was less than accurate. It often omitted the important qualifications that it was only homosexual men who were sexually active with multiple partners and that it was only Haitians who had recently immigrated who were being asked to exclude themselves.

The Red Cross's press release had been prepared quickly, in response to the announcement by the U.S. Department of Health and Human Services. Neither the gay community nor the Haitian community had been consulted before it was issued. The Red Cross had not approached representatives of high-risk groups and asked them to communicate the self-exclusion message to their groups. High-risk groups thus were not prepared for the Red Cross action.

Members of the Haitian community, particularly in Montreal, resented the implicit stigma and discrimination in being described as at high risk. Canadians of Haitian descent denounced the Red Cross's position as racist. A complaint was lodged with the Quebec Human Rights Commission. The Haitian Red Cross complained to the League of Red Cross Societies about the actions of the Canadian Red Cross and the American Red Cross. The Haitian embassy in Ottawa and the Haitian consulates in Toronto and Montreal protested to the Red Cross. Haitians picketed the Ottawa blood centre. Blood donor clinics in Montreal lost support. The Red Cross was particularly sensitive to the accusation that it was acting in a racist manner, an accusation that struck at the heart of its identity as a humanitarian and non-discriminatory organization. The accusation was also potentially damaging to efforts to recruit voluntary donors. All of this came at a time when the Red Cross was already facing criticism for shortages of blood in major cities.

Some homosexuals were offended by media reports that suggested that all of them had been designated as at high risk. They were concerned that serious repercussions would ensue if all homosexual men were identified as potential carriers of the AIDS virus. Members of the Toronto gay community discussed possible responses to the Red Cross press release at two meetings in March. At the first, attended by gay physicians, gay health workers, and gay journalists on 12 March, a consensus was reached that the Red Cross should ask prospective donors whether they had experienced any of the symptoms of AIDS but should not ask about sexual preference. Some participants criticized the definition of "sexually-active homosexual or bisexual men with multiple partners" as awkward, confusing, and subjective. It did not define how many partners counted as "multiple," nor would it necessarily encompass a "closeted" gay man who did not consider himself an "active homosexual." Another important issue was raised at the 12 March meeting:

There is a risk that closeted gay men, in social situations such as office blood drives, will feel they must give blood or risk being identified as gay. Should such men be advised of "legitimate excuses" (e.g., "I'm taking antihistamines") for refraining? It would be counter-productive to have members of an increased-risk group giving blood as a means of social self-protection!

Under the Red Cross system of donor screening there was little or no opportunity for a gay man who, for example, had been swept into a donor challenge, and whose co-workers or colleagues were unaware of his sexual orientation, to exclude himself or his donation without facing the potential embarrassment or discrimination that would come from revealing his sexual orientation. This was the situation that the confidential unit exclusion program at the New York Blood Center had been specifically designed to remedy by giving high-risk donors the opportunity to withdraw their donations from the blood supply without embarrassment.

At the second meeting with the leaders of the gay community in Toronto, on 22 March, it was decided that the gay community would not issue a public statement about blood donation in conjunction with the Red Cross. However, they agreed to "quietly endorse" the Red Cross's request for voluntary self-deferral of persons at high risk of infection.

The environment in which self-exclusion was introduced

In order to appreciate some of the difficulties and complexities involved in the implementation of voluntary self-exclusion, it is helpful to understand the nature and the history of the communities whose cooperation was sought.

During the 1950s, gay men had had places to meet but lacked a sense of community. Many gay men experienced isolation; many did not disclose their sexual orientation and pretended to be heterosexual. In the late 1960s, "gay liberation" emerged along with other social and civil rights movements. A turning point occurred in 1969 when, in New York City, the "Stonewall riots" occurred in response to a police raid on a gay night club in that city. It was the first occasion on which the gay community offered resistance to the police. Later that year, the first gay organization was founded in Toronto. Also in 1969, the Canadian Criminal Code was amended so that "buggery" and "gross indecency" were no longer criminal offences if the participants were consenting adults. In the years that followed, large gay communities emerged in Toronto, Montreal, and Vancouver, and smaller ones in Edmonton, Winnipeg, Saskatoon, Fredericton, and other cities. Increasing numbers of Canadians took part in gay social and political activities. Many gay persons "came out of the closet," making their sexual preference public.

Although a community in the sense of common social and cultural values emerged, it by no means included all homosexual men. Many chose not to live openly as gay men and remained "closeted" even as they engaged in homosexual sex. In his testimony, Edward Jackson, the editor of *The Body Politic*, a national gay tabloid, said:

I think it might be useful to think of it as a series of concentric rings with a group at the middle who are most visible, most identified with the community, most organized and then a series of kind of porous, if you like,

barriers and boundaries between them moving to other groups who are more or less identified and connected to that group. And the further away you got from that the less likely people would say they were part of a gay community, the less likely they were to say that they wanted to be involved in political or social activity.

And at the very extreme of that, which is a very broad range, I think you would find men who would have sex with men who did not identify at all. Who simply had sex, did not put a label on it and would certainly not say that they were gay.

The complex nature of the homosexual population in any centre made it difficult to communicate with all members to propose voluntary self-exclusion. It was difficult for persons at the "core" to communicate with persons in the "outer circles." For example, *The Body Politic* would not have reached many persons who did not consider themselves part of the gay community. They would not know where to find *The Body Politic*. They might be afraid to read it.

Bath houses developed out of the public bath houses that were common in the nineteenth century before all homes had private bathrooms. Some of these traditional bath houses continued to exist in the twentieth century. In the 1970s, the gay community became more active commercially and its members opened many more bars and bath houses. The bath houses contained private cubicles where gay men could meet and take part in anonymous sexual activity. They attracted men on the fringes of gay society – including married men – who wanted gay sexual contact but did not want to be identified as gay in the outside world. The bath houses were also an important symbol of sexual liberation for members of the gay community. Along with sexual liberation came an increased risk of sexually transmitted diseases, including hepatitis B. Before AIDS, however, most sexually transmitted diseases could readily be treated.

The 1970s, which brought about greater freedom for gay persons, also saw tensions grow between the gay community and its members and other persons and groups in the larger society. In November 1977, *The Body Politic* published an article entitled "Men Loving Boys Loving Men." Its publication led to the execution of a search warrant at the premises of *The Body Politic*. The police took away twelve cartons of documents, including the subscription list. Shortly after the search, the three officers of the corporation that published *The Body Politic*, including Mr Jackson, were charged with criminal offences. Eventually they were acquitted of those offences. At about the same time a twelve-year-old boy was murdered. The men who were accused of the murder were gay. The case attracted considerable public attention, and much of the hostility resulting from the revulsion over the murder became directed at the gay community.

In 1977 and 1978 the police raided bath houses in Montreal and Toronto and charged the occupants with being "found ins" in "common bawdy houses." During the Toronto raid, in 1978, the police seized the membership list of the bath house. The owners of the bath houses were acquitted. Most of the found-ins were also acquitted. Some pleaded guilty.

Bath house raids also occurred in Edmonton in the early 1980s. In February 1981, police raided four Toronto bath houses and arrested 266 men as found-ins. That action made many gay persons fearful of further stigmatization and discrimination. It also galvanized many in the gay community. Within twenty-four hours there was a street demonstration of several thousand people. They had considerable support from the non-gay community and the media.

This was the environment in which information about a strange new disease affecting homosexual men in the United States began to emerge in 1981. There was a suspicion in the gay community that the mainstream media were attempting to sensationalize the disease and that gay persons would become scapegoats. In particular, there was a concern that, in the absence of scientific evidence explaining the cause of the disease, the media were being quick to make moral judgments about gay men and their sexual practices. The media's reaction, it was feared, threatened the place in society of gay men and threatened the sexual freedom that many had come to enjoy and that had become a defining element of the gay community.

By the autumn of 1982, there was considerable controversy in the gay community over the question of whether its members should change their sexual practices. In November 1982, *The Body Politic* published an article entitled "The Real Gay Epidemic: Panic and Paranoia." The author, a professor of microbiology at the University of Toronto, was critical of the portrayal of AIDS in the mainstream media as spreading like "wildfire" and spreading from gay men to heterosexuals. He was also critical of suggestions that gay men change their sexual practices. He wrote:

If, as *TBP* [*The Body Politic*] writer Ken Popert believes, "promiscuity knits together the social fabric of the gay male community," then the diseases, the way they are being publicized – and the way we are reacting to them – have the potential for weakening that fabric by pushing us toward a new era of sexual conservatism.

The suggestion that promiscuity should be encouraged was vehemently rejected by others in the gay community who urged gay men to reduce the number of their sexual partners.

By early 1983, the likelihood that AIDS could be transmitted by blood had been used by some groups as a vehicle to promote discrimination against homosexuals. In January 1983 an anti-gay group called Positive Parents of

Canada called upon public health authorities to "publicly ask homosexuals to refrain from donating blood until a cure for AIDS [was] found." It also asked that public health authorities

undertake a program of inspection to insure that all known homosexually operated business of a public nature, such as Crispins Restaurant and the St Charles Tavern, employees undergo immediate health inspections to determine if they are AIDS carriers.

We furthermore recommend that notices be displayed in a prominent place in each of these businesses to advise patrons of the possible hazards involved in dining or drinking in such homosexual hangouts and that all homosexual steam baths (bawdy houses) be closed immediately and thoroughly inspected for any evidence of Herpes or AIDS that could be transmitted to casual visitors to such establishments who might be unaware that homosexuals are considered high risk carriers of Herpes as well as AIDS.

The organization also criticized the Red Cross in leaflets for refusing to "publicly designate homosexuals as a high-risk group" because it was "socially unpopular" and because it would "affect their donor recruitment programs."

Persons in the gay community were understandably sensitive to discrimination. Mr. Jackson wrote an article in *The Body Politic* about Positive Parents and, in the course of researching it during February 1983, asked Dr Derrick about the Red Cross's position with respect to the exclusion of homosexual men from donating blood. Mr Jackson's article appeared in the March 1983 issue of *The Body Politic*. It supported the Red Cross's position that it was "inappropriate" and "ineffective" to question blood donors about their sexual orientation. Dr Derrick was quoted as saying: "The evidence is not conclusive enough for us to change our blood-collection patterns. We are not taking any precipitous action." He was also quoted as saying that, if eventually it became clear that blood transfusions and AIDS transmission were related, it would then be necessary to institute stricter screening of blood donors by going to the leaders of the gay community for help in conveying information to potential donors and asking them not to donate.

It was in this highly sensitive and politicized environment that the Red Cross, an organization founded on the principle of non-discrimination, found itself when it launched its campaign of asking persons at high risk of contracting AIDS to refrain voluntarily from donating blood.

March–April 1983: Consideration of screening measures in Canada

On 24 March, the U.S. Food and Drug Administration issued guidelines that elaborated on the recommendations made earlier in the month by the Department of Health and Human Services. It recommended that blood banks

introduce educational programs to inform all donors about the groups that were considered at high risk and to ask persons falling within those categories to refrain from donating blood. It also recommended that they revise their donor questionnaires to include specific questions about symptoms of AIDS. Stricter guidelines were set out for those who sold their plasma, including the requirement that they be physically examined for lymphadenopathy, or swollen lymph glands, a symptom of AIDS, and for AIDS-related weight loss.

In Canada, the Red Cross local medical directors met in Toronto as scheduled on the same day, 24 March. Dr Derrick, who had recently come back from an AIDS conference in New York City, had sobering news for them. The number of cases of AIDS in the United States, at that time approximately 1,250, was expected to increase to at least 8,000 to 10,000 by the end of the year. Only 20 per cent of persons with AIDS had survived for more than two years. It was feared that the disease would move beyond the high-risk groups into the general population. One case in the United States had been linked to blood transfusion and fifteen others were thought to be linked.

Dr Derrick said that Canada was approximately one and a half years behind the United States in the development of the AIDS epidemic. That delay was important because epidemics usually progress at a rate that can be charted as a bell curve. At the beginning and end of the epidemic there are few new cases. The greatest number of new cases appear at the middle. The fact that the epidemic in Canada was one and a half years behind the epidemic in the United States meant that there was in Canada an opportunity to prevent many cases of AIDS.

Some medical directors reported that they had been taking measures of their own to exclude donations from persons believed to be at high risk of transmitting AIDS. In British Columbia, for example, nurses who suspected that a donor belonged to a high-risk group tagged the donation, withdrew it from the system, and later destroyed it. Other medical directors used similar procedures to identify suspect donations for destruction.

The minutes of the medical directors' meeting contain the following statement:

Dr. Perrault stated that blood collected from high risk group donors is not to be singled out at the moment. Some Centres had it held in Quality Control testing and others had disposed of it.

Whether this minute, written by Dr Perrault, accurately reflected his comments on the issue was the subject of conflicting evidence. Dr Perrault testified that he did not say that suspect donations should not be specially marked. He testified that he told the medical directors only that the donors of suspect donations should not be identified in their donor records as having

had their donations rejected. He said he was concerned that if donors were identified in this manner, they would be rejected on subsequent donations but would not know why they were being rejected.

It is difficult to reconcile Dr Perrault's explanation with the plain meaning of the minute, which in turn is supported by the fact that the policy for exclusion of high-risk donors at the time was entirely by voluntary self-exclusion. The Red Cross did not have a policy requiring Red Cross employees to exclude persons at high risk who did not voluntarily self-exclude, nor did it have a policy that donations from such persons would not be used. Nor would Red Cross employees who referred to the donor criteria manual find any direction in that document to exclude persons believed to be at high risk of contracting AIDS who had not voluntarily withdrawn from donating.

Dr Perrault's explanation is also contradicted by the evidence of Dr Thomas Bowen, the medical director of the Calgary blood centre. Dr Bowen understood that medical directors had been told not to mark suspect donations in any special manner. Nevertheless, from the summer of 1983 to the autumn of 1985 the Calgary blood centre continued to use a "black dot" procedure; if a donor appeared unwell, had new tattoos, or was suspected of being at high risk of contracting AIDS, nurses marked the donation with a black dot to signify that it was not to be used for transfusion. Dr Bowen felt that this ought to be within the discretion of nurses with solid clinical judgment. He did not tell the national office about this practice, which he believed to be sound, because it did not conform to what he believed to be the policy of the national office that donations of persons at high risk who had not self-excluded were to be used. He did not tell the national office of his practice because he did not want to be told to stop.

At their meeting on 24 March, the medical directors also discussed the issue of questioning donors about symptoms of AIDS. Dr Derrick had prepared the following list of AIDS-specific questions to be included in the donor questionnaire:

Are you feeling well? If not:-

- | | |
|-------------------------------------------|-----------------------------------|
| 1. Weight loss – unintentional? | No. of pounds lost
in how long |
| 2. Diarrhea for more than one week? | |
| 3. Fever for more than one week? | |
| 4. Cough for more than one week? | |
| 5. Night sweats? | |
| 6. Shortness of breath? | |
| 7. Extreme fatigue? | |
| 8. Swollen glands for more than one week? | |
| 9. Sore throat for more than one week? | |

10. Difficulty swallowing for more than one week?
11. Cold sores (painful blisters in mouth or lips)?
12. Thrush (white patches in mouth)?
13. Any new skin lesions?
14. Any other symptoms you would like to ask about?

One medical director had already added questions about such AIDS symptoms as unexplained night sweats and swollen glands to his centre's donor questionnaire. The consensus of the medical directors was that these were acceptable questions. The minutes record, however, that Dr Davey told the medical directors that

no Centre should be asking any questions other than the basic: "Are you well?" and most definitely, no Centre should be conducting its own diagnostic quiz for AIDS.

The medical directors concluded their discussion of AIDS by calling for the creation of a working group to deal with all issues relating to the Red Cross and AIDS. The working group was to meet for the first time on 29 March.

On that day, the AIDS working group met in Montreal. It consisted of Dr Derrick, Dr Perrault, three of the local medical directors, the national coordinator of public relations, and the national director of nursing. Also present were some invited guests, including Dr Denise Leclerc-Chevalier, the executive director of the Canadian Blood Committee, the body through which the provinces funded the blood program, and Michael Worsoff, a member of the board of directors of the Red Cross and its honorary counsel. The meeting first dealt with the Red Cross's concern about its legal position if it prevented persons at a high risk of contracting AIDS from donating, and the amount of evidence that would be required for it to exclude such persons from donating blood. The minutes record the following discussion:

[Dr Perrault] referred the subject matter to Mr. Worsoff with the question "What would be the legal aspects if an issue is made of the right of donors to give blood?" Mr. Worsoff stated that it is not a matter of the donor having a right to donate blood rather it is a case of the Red Cross having both a moral and legal obligation to assure the safety of the blood it accepts for processing and distribution. The evidence of possible unacceptability of the blood does not have to be conclusive – the decision can be made on a basis of "reasonable doubt" as to its suitability. With reference to the AIDS problem in particular, the premise is not that the CRC [Canadian Red Cross] has to justify beyond any scientific doubt that there is a link between the designated "high risk groups" and the development of AIDS since, if there is even a possibility of transmission via blood, CRC has the moral and legal obligation to protect the blood recipient above all.

The working group went on to consider whether questions about symptoms of AIDS should be added to the donor questionnaire. This had been recommended in the U.S. joint statement of 13 January 1983, and had been the first of the additional measures the Red Cross had undertaken to carry out in its press release of 10 March 1983. Despite that public position, the statement to the Canadian Hemophilia Society on 7 February, the position expressed by the Red Cross in its press release on 10 March, and the consensus of medical directors five days earlier, the working group decided that specific questions about AIDS symptoms would not be asked and that the only change to be made would be in the preamble. The minutes read as follows:

A decision was reached that the present questions were adequate for ascertaining that the donor was in a state of good health and that any further questions could not be sufficiently specific to determine whether or not a donor might be in the early stages of AIDS.

It was agreed that the preamble to the questions be revised to emphasize the obligation of the donor to read and answer carefully all the questions pertinent to establishing that he/she was in a state of good health. The Medical Directors present at the meeting reframed the preamble to read as follows:

1st paragraph:

"Thank you for your gift of blood. In order to protect you and the recipient of your blood, it is important that you be in good health. Please read these questions carefully each time you give. If your answer is yes to any question, notify the nurse."

2nd paragraph:

"A yes answer does not necessarily disqualify you as a donor."

There was no difference in substance between the new questionnaire and the one used before the emergence of AIDS. There was no suggestion that persons at high risk of contracting AIDS should refrain from giving blood. Any mention of AIDS or AIDS symptoms was conspicuously absent. This was a significant departure from the earlier Red Cross undertaking to ask donors about the symptoms of AIDS. As a result of the working group's decision, no donor screening for AIDS or donor education about AIDS took place at most blood clinics in Canada for more than a year.

The working group decided that the Red Cross would "develop a dialogue" with high-risk groups in order to promote a better understanding of the policy of self-exclusion. With respect to public relations, it decided that no new press release would be issued because there was "no new medical evidence, information, or change in CRCS [Canadian Red Cross Society] position to warrant such a release." In fact, there had been a change in position because of the decision not to ask about symptoms. The change was not publicly

disclosed, in part, at least, because the Red Cross did not want to revive the controversy that followed its previous release by restating publicly that recent immigrants from Haiti should exclude themselves.

On 8 April 1983, Dr Derrick met representatives of Toronto gay organizations. He was told that gay organizations had been making a concerted effort to convey information about AIDS to gay men and that the production of a pamphlet on AIDS, which included advice about refraining from blood donation, had recently been completed by a group called Gays in Health Care. The gay representatives expressed their concern about the media coverage of the Red Cross's request for self-exclusion by high-risk groups. They said that newspaper articles and other media reports were biased, with the consequence that conscientious gay blood donors had developed hostile feelings towards the Red Cross. The gay representatives were asked to provide a list of names of gay activists throughout the country who could be approached by the local Red Cross medical director, and asked to explain the policy of self-exclusion to others in their community. Some of those attending tried to explain to Dr Derrick that it was unreasonable to assume that gay leaders would be able to communicate the message of self-deferral to all gay and bisexual men.

The advisory committee of the Red Cross blood transfusion service met on 15 April 1983. This was an important committee. Both the chair and vice-chair were members of the board of directors of the Red Cross, and the chair was a member of the executive committee of the board. The advisory committee reported to the board of directors and gave it technical advice about the blood program. Many of the voting members of the advisory committee were experts in transfusion medicine, and none was an employee of the Red Cross blood transfusion service.

Dr Davey asked the advisory committee to endorse the new Red Cross questionnaire, which did not ask donors AIDS-specific questions but only emphasized in its preamble that the donor should be in good health. Several members of the committee raised the issue that the Red Cross, by not asking specific questions about symptoms, was retreating from its earlier position. Dr Davey characterized the new general preamble as a "modification" of the earlier position, but said this had been done with "a view to practical effectiveness, and with the agreement of all B.T.S. [blood transfusion service] Medical Directors."

In fact, unlike the consultation with the medical directors in February, when they were asked whether the U.S. joint statement should be adopted, in this case the medical directors had not been asked whether it was sufficient to change the preamble of the questionnaire without adding specific questions about AIDS. Dr Davey explained in his testimony that he believed that he had the "agreement of all" medical directors because they had all received copies of the minutes of the 29 March meeting of the ad hoc working group, and because it was standard practice for the two medical directors who

attended the advisory committee meeting to canvass all the other medical directors, before it met, in order to learn of any concerns that should be brought to the advisory committee. No such concerns were expressed at the meeting. However, even if the minutes of the ad hoc working group had been prepared and sent to all medical directors in the seventeen days before the advisory committee met on 15 April, it is not probable that all medical directors would have read them and appreciated the change in policy. At most, there was a lack of formal objection from persons who might not have known that such a decision had been taken and who had supported the addition of AIDS-specific questions at a meeting less than a month earlier. In these circumstances, the lack of formal objection could hardly be interpreted as unanimous agreement. The advisory committee voted to endorse the approach of the Red Cross.

On 28 April, Dr Derrick wrote to the local medical directors and included a summary of his meeting on 8 April with representatives of the gay community. The summary described the Red Cross policy under which the medical directors were to communicate with representatives of the gay community in their areas. Dr Derrick said that the names of "contact individuals" in the gay community would be sent in early May. The medical directors were not directed or encouraged to do anything about communicating with the gay community before they received those names.

May 1983: Creation of the National Task Force on AIDS

By the beginning of May 1983, twenty-four cases of AIDS had been reported to the Laboratory Centre for Disease Control in Ottawa. In the United States, 1,361 cases had been reported to the Centers for Disease Control, and an additional 100 cases were being analysed.

On 5 May 1983, the first meeting of the National Task Force on AIDS took place. This group, which was later called the National Advisory Committee on AIDS, was appointed by the Minister of National Health and Welfare to advise her and the Department of National Health and Welfare about AIDS issues. Its membership consisted of scientists in the fields of epidemiology, immunology, and virology and representatives of the Red Cross, the Department of National Health and Welfare, and the Canadian Blood Committee.

Dr Derrick attended the meeting of the task force on behalf of the Red Cross and sought its "endorsement" of the measures that the Red Cross proposed to take, as described in the press release of 10 March 1983, to reduce the risk of transmission of AIDS through the blood supply. It was unusual for the Red Cross to seek the endorsement of an outside body of measures taken within its responsibility for protecting the blood supply. The Red Cross had no shortage of internal committees and had many highly qualified external experts on its blood transfusion service advisory committee. It sought the endorsement because it wanted the agreement of a respected, external

body that it had not engaged in discrimination in identifying recent Haitian immigrants and some homosexuals as being at high risk of contracting AIDS. The task force passed the following resolution:

That the National Task Force on AIDS endorsed the press release of the Canadian Red Cross Society (10 March 1983) and supported the recommendations made therein. It was considered that the Society acted in a prudent and non-discriminatory manner; it was unfortunate that the recommendations had been misinterpreted, especially to segments of the Canadian population whose members had victims of AIDS.

The task force was not told that the Red Cross had changed its publicly stated position on asking donors if they had symptoms of AIDS. Only two of the persons attending the meeting of the task force, the executive director of the Canadian Blood Committee, Dr Denise Leclerc-Chevalier, and the director of the Laboratory Centre for Disease Control, Dr Alastair Clayton, had attended the meeting of the Red Cross blood transfusion service advisory committee on 15 April 1983. They would have learned at that time of the Red Cross's decision not to ask questions about symptoms, despite its earlier endorsement of the U.S. joint statement that recommended such questions.

May–June 1983: Consideration of the level of risk and of confidential unit exclusion

The volunteer U.S. blood collection agencies had taken steps in January 1983 to question donors about symptoms of AIDS. In March 1983 they began to tell all potential donors, when they came to the clinic, about the groups considered at high risk of contracting AIDS and that it was important that members of those groups refrain from giving blood. They did so simply and easily by giving potential donors a pamphlet about AIDS. By May 1983, the American Red Cross had found that the pamphlet had not made the donation process more difficult. The number of donations remained constant.

That month, Canadian Red Cross officials began to consider preparing a similar pamphlet for Canadian donors. Its development was impeded, however, by a fear among the blood donor recruitment employees and volunteers that printed information about AIDS, listing the high-risk groups, would offend some donors, who would leave the clinic immediately or not return to donate again. This concern was not based on any study or survey of donors' attitudes.

On 20 May 1983, Dr Derrick wrote to Dr Perrault and Dr Davey about a forthcoming meeting with City of Toronto public health officials. He suggested that the Red Cross prepare an information pamphlet "to be used as local concerned groups see fit should the epidemic show signs of worsening."

The meeting, which had been requested by the public health officials, took place on 26 May. William Mindell, the city's coordinator of community health information, reported to his colleagues what he had learned from Dr Derrick at the meeting:

The CRC BTS [Canadian Red Cross blood transfusion service] medical advisory committee is very conservative and won't threaten the system they've developed. John Derrick feels public pressure may yet force more overt precautionary measures on the part of the donor clinics within the next few months (confidential opinion) ...

They were still reeling from their public statements regarding Haitian donors and the clamor it had caused re: defending against charges of racism. It had occupied a tremendous amount of their time and they had little interest in going through it again (and little experience in media relations on controversial topics!). They noted that the situation had calmed, but they were still not able to agree on a joint statement to be issued with the Haitian community.

On 30 May, Dr Davey wrote a memorandum in which he attempted to calculate "the incidence and risk of AIDS associated with blood transfusion in the U.S." Dr Davey, who was not an epidemiologist, took the number of reported transfusion cases that had met the definition of AIDS developed by the Centers for Disease Control and, on the assumption that the cases had occurred over three years, calculated the "incidence" by dividing this number by the number of blood transfusions in the United States during that period. Dr Davey concluded that the incidence of transfusion-associated AIDS was 1.5 cases of AIDS per million transfusions. He concluded that "the risk of AIDS associated with transfusion is very low and may not even be significant."

Dr Davey's calculation of risk did not take into account persons infected through transfusion who were in the preliminary stages of the disease but did not meet the full diagnostic definition of AIDS. Nor did it take into account the lengthy latency period of the disease, that is, the fact that there would be persons infected through transfusions who had not yet developed symptoms of AIDS. To use a common simile, by this time the AIDS epidemic was like an iceberg. The diagnosed cases of AIDS were the part of the iceberg that could be seen above the water-line. The persons who were infected but were still asymptomatic, or were showing only precursor signs of AIDS, were the much larger part of the iceberg, below the water-line. Dr Davey's calculation accurately represented the prevalence, or number of current and known cases, of AIDS among blood transfusion recipients, but it was an inaccurate representation of the risk of infection from the blood supply. While the prevalence was calculated from the tip of the iceberg, the risk should have been

calculated using the whole iceberg. The whole iceberg could not be estimated accurately at the time, but it was clearly much larger than the tip, making the risk much more significant than Dr Davey's estimate.

New information about AIDS infection through blood and blood products was discussed at a meeting of the American Blood Resources Association in Washington, DC, from 7 to 9 June. Dr Derek Naylor, director of the Canadian Red Cross blood products services, attended. During the meeting, Dr Louis M. Aledort, a medical adviser to the National Hemophilia Foundation, reported that in the United States thirteen hemophiliacs, who had no other risk factors, had been diagnosed as having AIDS and an additional ten cases were being evaluated. He said that attempts should be made to prevent persons at high risk from donating, but that it must be recognized that the efforts would not be completely successful. Dr Henry Masur of the National Institutes of Health made a presentation on the scientific and clinical manifestations of AIDS. He described the precursor states of persons believed to be infected with the agent causing AIDS and said that homosexuals suffering from generalized lymphadenopathy, homosexuals with no symptoms other than immune deficiency, and hemophiliacs with immune abnormalities might go on to develop AIDS. He said that it was possible that a large reservoir of individuals existed who did not have AIDS but who harboured its causative agent. These persons might feel well and presumably would not be dissuaded by a questionnaire that emphasized the importance of feeling well.

During this meeting, the Canadian Red Cross learned about the confidential unit exclusion program developed by the New York Blood Center, which allowed high-risk donors to ensure without any public disclosure that their donations would not be used for transfusion. The New York Blood Center reported that its donations had been reduced by 14 per cent since mid-March. Only a portion of this decrease was attributable to the confidential unit exclusion. Three per cent of the donors at its clinics had either excluded themselves or designated their donations as not to be used for transfusion. Six per cent of donors had stopped attending the clinics. An additional 5 per cent had been deferred as a result of AIDS-specific questions about their health. Before AIDS-specific questions were asked, approximately 15 per cent of donors had been rejected "on medical grounds." After the addition of AIDS-specific questions, the proportion of persons deferred for all medical reasons rose to 20 per cent.

Dr Davey testified that confidential unit exclusion was not a measure that appealed to the Canadian Red Cross Society. The Canadian Red Cross did not know whether confidential unit exclusion was an effective measure. It believed that the epidemiological situation in Canada was very different from that in New York. It was concerned about a potential loss of donors – something he said that the New York Blood Center did not have to be concerned about because it could always purchase red cells from elsewhere in the United States or from Europe, if necessary.

July 1983: Communications with representatives of the gay community

On 28 April, Dr Derrick had written to the medical directors of the seventeen Red Cross blood centres, telling them about his meeting with representatives of the gay community in Toronto three weeks earlier and saying that he expected to receive a list of contact persons in gay communities by early May. He did not in fact receive the contact names until 14 July 1983. On receiving them, he wrote to the local medical directors as follows:

Obtaining the list turned out to be a much longer procedure than anticipated, in fact I only received an incomplete list today. In all probability by this time you will already have made contact with somebody suitable in your area but for what it is worth the names for your region which have been provided me are ...

Dr Derrick was able to write in this manner to only some of the medical directors. He had not received names of contact persons in Regina, Sudbury, Montreal, Quebec City, Saint John, St John's, or Halifax. Dr Derrick did include with his memorandum, however, a copy of an article in *Canadian Doctor* magazine that listed the names and telephone numbers of gay support groups, including those in Regina, Quebec City, and Montreal. The medical directors in Quebec City and Montreal testified that they did not receive this memorandum.

It is not clear what the basis was for Dr Derrick's belief that the medical directors had already "made contact with somebody suitable." There had not been any previous written direction for them to do so. They had merely been told, at the end of April, that contact names would be forthcoming. Medical directors who had not yet contacted gay community representatives were instructed in the memorandum to do so in order to explain that the Red Cross expected the groups to spread the message of voluntary self-exclusion. There was no direction to do anything more than communicate that expectation. Medical directors were not asked to assist the local gay organizations, most of whom had meagre resources, to disseminate the message of self-exclusion.

Several medical directors had made efforts to communicate with members of the gay community in their communities even before they received Dr Derrick's memorandum of 14 July. Dr Richard Huntsman, the medical director of the St John's blood centre, met with representatives of the Gay Association in Newfoundland on 21 March. Dr Huntsman and the representatives reached an agreement. The Red Cross, in Newfoundland, would not publicly say that homosexuals were at high risk of contracting AIDS. In return, members of the gay community would not donate blood.

Dr Marlis Schroeder, the medical director of the Winnipeg blood centre, met with members of the gay community in Winnipeg on several occasions

to give them information about AIDS and to ask that gay persons refrain from donating blood. She took this initiative before receiving Dr Derrick's memorandum of 14 July 1983. Dr Schroeder also stated her support for an AIDS pamphlet prepared by the gay community in Winnipeg that encouraged gay persons not to donate blood. Dr Schroeder did not, however, suggest that it be circulated at Red Cross blood donor clinics. The pamphlet contained the following statement:

Men who are not "out" to members of a group with whom they donate blood (e.g., work) can phone [the Winnipeg blood centre] and ask for Dr Schroeder or Miss Catherine Anderson and request that the blood which they just donated be used "for research purposes only."

Dr Brian McSheffrey, the medical director of the Saskatoon blood centre, met with a gay community representative as early as February 1983 about the dissemination of the self-deferral message. He found the "gay hot line" in Saskatoon simply by looking in the telephone book. Dr Thomas Bowen, the medical director of the Calgary blood centre, and Dr Anita Ali, the deputy medical director of the Hamilton blood centre, took steps in July 1983, following receipt of Dr Derrick's memorandum, to make contact with gay community representatives in their areas.

Medical directors in Saint John, Montreal, Quebec, and Halifax did little or nothing to communicate with gay community members in their areas. Dr John MacKay, of the Saint John centre, had not received any contact name from the national office and knew of no gay organization in New Brunswick. His only effort to communicate with the gay community was to look in the Saint John telephone directory for a gay organization. He did not look in any telephone directories for other New Brunswick cities. At the time, there was an organization called Fredericton Lesbians and Gays. Its telephone line, called "Gayline," was listed in the Fredericton telephone directory, although not in the Saint John directory.

Dr Raymond Guévin, the medical director of the Montreal blood centre, did not contact the gay community there. He testified that he believed that groups within that community were well informed and that he did not believe that his communications would be welcome. He said that his deputy medical director had been given the responsibility for contacting the gay community but Dr Guévin could not recall when such contact took place. Members of the Montreal gay community testified that they did not hear from the Red Cross until 1987. Dr Joseph-Ernest Côme Rousseau, the medical director of the Quebec City blood centre, made no efforts to communicate with the gay community in that city.

In Halifax, Dr Max Gorelick, the medical director of that city's blood centre, considered the memorandum from Dr Derrick a "recommendation." He did not communicate with the person whose name had been given to him or

with anyone else in the gay community until 1985. Dr Gorelick was quoted, however, in an article in the *Halifax Daily News* of 25 April 1983 as confirming that the Red Cross had "issued a national request that people in an AIDS high-risk group not give blood."

Communication with the gay community was a key element of the Red Cross program to encourage the voluntary self-exclusion of donors at high risk. Both Dr Perrault, the national director of the blood transfusion service, and George Weber, then the secretary general of the Red Cross, agreed that, if it had come to their attention that some medical directors were not communicating with representatives of the gay community, they would have taken steps to ensure that they did so. After Dr Derrick wrote his memorandum in July 1983, there was no supervision or follow-up to confirm that medical directors had communicated with representatives of the gay community. For their part, the medical directors who were not successful in communicating with gay representatives, or who took no steps to do so, did not report this to Dr Derrick.

July 1983: A second press release from the Canadian Red Cross

On 19 July 1983, a press conference was held to announce the formation of the AIDS Committee of Toronto, an organization concerned with local AIDS issues, including the support and counselling of patients, education within the gay community, fundraising, political action, and media liaison. Taking part in the press conference were public health officials and Dr Herst, the deputy medical director of the Toronto blood centre.

Dr Herst had been given draft answers for questions that were expected at the press conference. The answers had been written by Dr Derrick in collaboration with Dr Davey and Dr Perrault. They had revised a draft of questions and answers prepared by the City of Toronto's public health department. With respect to the definition of high-risk groups, the answer was as follows:

Homosexuals and Haitians should be, and are, allowed to donate blood in Canada provided they meet the existing selection criteria required of all blood donors. However, because of uncertainties currently surrounding this issue, homosexuals and recent immigrants from Haiti are being advised not to become blood donors at this time.

The type of homosexual behaviour that should give rise to self-exclusion was dealt with in another draft response:

The degree of promiscuity has ceased to be a factor since cases are now known where a single intimate contact has resulted in AIDS development. Until more is known, individuals belonging to groups at higher than normal risk of developing AIDS are advised to refrain from donating blood.

This was a much broader definition of homosexual behaviour leading to high risk than had been articulated in the press release in March. That press release had referred to "sexually-active homosexual or bisexual men with multiple partners." The new recognition of danger in single homosexual contacts was consistent with the evolving knowledge of AIDS and its transmission. It was now recognized that the number of sexual partners was not an essential factor in determining the risk for AIDS, and the draft answer was consistent with a new description of risk groups released on 24 June 1983 by the Centers for Disease Control. The week before the press conference, on 12 July, Irwin Memorial Blood Bank in San Francisco had instructed its staff to interpret "multiple partners" as "more than one"; gay men would be eligible to donate there only if they had been monogamous for three years with another monogamous partner. The period of three years was chosen because the most recent knowledge at that time was that AIDS might have an incubation period of three years.

At the press conference, Dr Herst was questioned by representatives of the media about who should refrain from donating blood. She said that it was the Red Cross's "unofficial policy" to discourage homosexuals from donating blood. Her comments were reported over the next few days in the media.

The reports angered members of the Toronto gay community, who had not been made aware of any Red Cross policy, unofficial or otherwise, of discouraging all homosexual men from donating blood. On 20 July, the day the first of the reports appeared, a meeting took place between the AIDS Committee of Toronto and the Red Cross. The Red Cross said at the meeting that there had been no change in its definition of high-risk groups. After the meeting, the AIDS Committee of Toronto issued a press release that contained the following statement:

A second development since yesterday morning concerns the erroneous and distorted reports of the position held by the Canadian Red Cross concerning blood donations from gay men. Today in an emergency meeting with ACT [AIDS Committee of Toronto] and the Toronto Department of Public Health, the Red Cross informed us that its blood donor policy set last March 10 has not changed, although it is, as usual, under review in the light of incoming scientific information about AIDS.

The Red Cross was sensitive to the fact that Dr Herst's comments, although scientifically sound, had angered the community at which the message of self-exclusion was directed. Dr Davey testified that there had been a concern in the Red Cross that, if some members of the gay community felt sufficiently provoked, they might donate blood out of protest. At this time, no gay person in Canada had ever made such a threat. The Red Cross was also sensitive about offending donors and potential donors. The summer was traditionally the worst time for shortages, and 1983 was the worst year for collections in five years.

Two days later, on 22 July, the Red Cross issued a press release that reiterated that the risk groups were

sexually-active homosexual or bisexual men with multiple partners, current or past intravenous drug abusers, recent Haitian immigrants, patients diagnosed with AIDS, sexual partners of AIDS patients, persons with AIDS symptoms, and sexual partners of individuals at high risk for AIDS.

That statement reignited the dispute with the Haitian community. The Red Cross and representatives of the federal government had previously met with Haitian community representatives in an attempt to address their concerns and resolve complaints about human rights. A "joint communiqué" had been drafted reporting the resolution of the dispute between the Haitian community and the Red Cross. After the second press release, the communiqué was never signed by anyone on behalf of the Haitian community.

The Red Cross continued its policy of voluntary self-exclusion. On 25 July 1983, the nurses at the Toronto blood centre were instructed that persons who identified themselves as being at high risk should be given the opportunity to speak to a nurse and be "encouraged to defer themselves." The nurses were given no direction about the course to be followed if high-risk donors insisted on donating.

By the end of the summer of 1983, the Red Cross's program of encouraging self-exclusion consisted of the two press releases and the communications with members of the gay community referred to earlier. The effectiveness of its public information campaign in disseminating the message of voluntary self-deferral was described in a memorandum written by the assistant national coordinator of public relations on 29 September 1983:

Examination of our clipping files reveals that only three newspapers, *Le Soleil* (Québec City), *Le Devoir* (Montréal) and *La Tribune* (Sherbrooke) picked up the release of March the 10. However, a March 9 interview with Dr Derrick by the *Globe & Mail* on the same subject was picked up by the wire service and reported widely across Canada on all media. The July 22 release, which was issued because of confusion arising from an earlier press conference at Toronto City Hall, was issued nationally but picked up chiefly in Toronto, where the confusion originated. The *Globe & Mail*, the *Toronto Star*, and the *Niagara Falls Review* ran short stories based on the release, with the main point a clarification of which homosexuals should not give blood at present.

In all likelihood, these releases were picked up by radio and TV, in particular the release of March 10, but we have no monitoring system for broadcast media and cannot give a clear indication in this area.

In his testimony, Dr Perrault agreed that the coverage in the print media was limited. He agreed that the lack of strenuous efforts to create a general public information campaign to discourage persons at a high risk of contracting AIDS from donating was based, at least in part, on a concern that such a campaign would frighten away donors.

Community-based measures to prevent contamination

With few exceptions, homosexual men and gay organizations did not reject or protest against the Red Cross strategy of voluntary self-exclusion. On the contrary, despite the lack of communication with, direction from, or assistance by the Red Cross, in most parts of Canada AIDS-related organizations, gay organizations and publications, and physicians serving the gay community made considerable efforts to tell homosexual men at high risk of contracting AIDS that they should not donate blood. Their efforts began in the spring of 1983, in some cases before the Red Cross decided to discourage blood donations from persons at high risk, and continued through 1985 after the Red Cross began testing blood donations for the antibody to HIV. The organizations that carried out this work had few resources to devote to the task. Governments provided few funds to community-based AIDS organizations until the latter part of the 1980s.

Community-based educational efforts of this kind were most organized in urban centres with large gay populations, of which Vancouver, Toronto, Winnipeg, and Halifax are examples.

Vancouver

In the early 1980s, Vancouver had one of the largest and best organized gay communities in Canada, centred in the district known as the west end. Four physicians who practised there provided medical services to most of the gay persons in the district. In 1981 and 1982, they began to notice patients with swollen lymph glands and unusual skin infections and suspected that the symptoms might be associated with a disease, newly identified in the United States, that came to be known as AIDS. An AIDS care team was created at St. Paul's Hospital in order to exchange information. The physicians on the team recommended to their gay patients that they have fewer sexual partners and refrain from donating blood.

In February 1983, a group of gay men formed AIDS Vancouver, a non-profit organization with the following purposes: to act as a liaison with the residents of the city, physicians, and government; to disseminate accurate information about AIDS, its symptoms, diagnoses, and treatment; to promote research into the cause and prevention of AIDS; and to provide support services to persons with AIDS. It was the first group of its kind in Canada. One of its first activities was to organize a public forum about AIDS, which

was held on 12 March 1983 and was attended by about 300 persons. At that meeting, gay men who were sexually active were advised not to donate blood. The forum, and that advice, were reported in the April issue of a newsletter published by the Vancouver Gay Community Centre, together with a suggestion that gay men find lesbians, a group at low risk for AIDS, to donate blood in their place.

AIDS Vancouver devoted a significant amount of effort to public education. It held several other forums that were well attended by members of the gay community. Representatives of it spoke at gay bars and bath houses and held monthly meetings at the Lotus, a gay club in Vancouver, where they distributed information, including advice not to donate blood. In late 1984 and early 1985, AIDS Vancouver produced a poster that was displayed in bath houses and bars frequented by gay men. It said, "If you're here ... Don't give blood, now, more than ever" and warned that recipients of blood transfusions might become infected with HIV. Should that happen, the poster said, there could be "dangerous repercussions" for gay men. The poster announced that the Red Cross would soon be able to test blood donations for the antibody to HIV and that the results would not necessarily be confidential.

The medical directors of the Red Cross's Vancouver blood centre were aware of the efforts of the Vancouver gay community, AIDS Vancouver, and physicians serving the gay community to encourage sexually active homosexual men not to donate blood.

AIDS Vancouver had few resources. Although it received some money from the federal government and the City of Vancouver, it did not receive stable funding from the provincial government until 1987.

Toronto

Gays in Health Care, a group of gay physicians, dentists, psychologists, and social workers, was organized in the spring of 1982 in Toronto to serve the health care needs of gay persons. In its spring 1983 newsletter, it reported that more than 840 cases of AIDS had been identified worldwide, sixteen of them in Canada; that three-quarters of those infected were sexually active gay or bisexual men; and that other persons at risk of contracting AIDS were recipients of many transfusions of blood and blood products, intravenous drug users, and Haitians. Enclosed in the issue was a statement by the American Association of Physicians for Human Rights, a group of gay and lesbian physicians with practices of gay and lesbian patients, advising gay men to reduce the number of their sexual partners and urging high-risk groups not to donate blood. An editorial comment in the issue described that statement as "premature, alarmist and without substantiation" and said that it did not represent the opinion of Gays in Health Care. The organization changed its position after

the Red Cross issued its press release in March asking gay men with multiple partners not to donate blood. A pamphlet about AIDS distributed by Gays in Health Care in April 1983 contained the following message:

Since AIDS may be transmitted through blood, the Canadian Red Cross has asked groups they feel are at high risk to refrain from donating blood. These include individuals exhibiting any of the known AIDS symptoms and sexually active gay men with multiple partners. In Canada, it is believed that the risk of transmission through blood transfusions is very low and no AIDS cases have yet been reported. However, the Red Cross wishes to take this cautious measure temporarily until a test is developed to identify blood which may carry an AIDS infectious agent.

In April 1983, the AIDS Committee of Toronto, consisting primarily of gay persons, was established as a non-profit organization for health promotion. It created six subcommittees, one of which was responsible for reviewing current medical literature in the field and for educating physicians about AIDS. Another subcommittee was responsible for educating the gay community; it decided that the best way to do so was by "a soft sell, non-judgmental approach with emphasis on general information, risk symptoms, and referral information." The AIDS Committee of Toronto organized two public education forums in 1983. In June, approximately 800 persons heard a panel of physicians present information about AIDS and then participated in small group discussions of particular issues. Various articles and pamphlets were distributed, including one of the committee's own brochures, *Gay Sex and AIDS*, which included the following information:

The actual cause of AIDS isn't known yet, but it is strongly suspected to be a virus-like agent which is transmitted in bodily fluids. Most cases in gay men were probably sexually transmitted, though some may have been caused by sharing hypodermic needles. Blood and semen almost certainly can carry AIDS, while saliva, rectal mucus, urine and sweat may carry it.

A new case of AIDS may begin when semen, blood, or another bodily fluid carrying the agent enters the bloodstream.

The AIDS Committee of Toronto published a monthly bulletin intended to inform the gay community about developments in the field and to disseminate public health information. In January 1984, for example, the bulletin discussed the similarities between hepatitis B and AIDS; it said that both could be transmitted by blood or semen and that gay men, hemophiliacs, users of intravenous drugs, and health care workers were at high risk of transmitting AIDS. In February 1984 it featured an article on hemophiliacs and AIDS that discussed the advantages of cryoprecipitate over factor concentrates and the relative safety of Canadian and U.S. blood products. In

May 1985 the bulletin reported on what it said was the first person in Canada to contract AIDS from a blood transfusion, a resident of British Columbia who had received a transfusion three years earlier after a car accident.

The AIDS Committee of Toronto had severely limited resources in the early 1980s. The government of Ontario gave it some limited funds in 1984, but it was not until September 1985 that it received stable financial support from the provincial government.

Winnipeg

During the early 1980s, the Manitoba gay community and health care professionals undertook some of the most extensive efforts in Canada to urge gay men not to donate blood. Some of the health care professionals formed a group after reading, in the 10 December 1982 issue of the *U.S. Morbidity and Mortality Weekly Report*, about a person who was diagnosed as having AIDS after a blood transfusion. Like their colleagues in other provinces, they tried, with the limited medical knowledge of early 1983, to take measures to limit the transmission of the disease. They began to ask questions about past blood donations when they took patients' histories and urged persons at high risk of contracting AIDS to refrain from donating blood.

The Manitoba Gay Coalition, a gay rights advocacy group, began distributing pamphlets in August 1983 to gay bath houses and bars, and, through the mail, to gay organizations. Its printed material was available in rural as well as urban areas. Its publications urged members of high-risk groups not to donate blood and emphasized that, in the interests of safety, it was necessary to assume that AIDS had a long latency period. The coalition sponsored an AIDS forum in August 1983 that was attended by hundreds of gay men. During it, a pamphlet was distributed recommending caution:

In order to make correct decisions about blood donation, ideally we should be able to draw on clear factual information. However, with the incomplete information we currently have and with the seriousness of AIDS, it is better to be perhaps overly cautious in our recommendations than to find out later that we have not been cautious enough.

The pamphlet stated that there were legitimate grounds for believing that AIDS might be transmitted by blood or plasma donated by persons who appeared and felt perfectly healthy, but in fact were "incubating" the disease. It went on to say:

As yet, there is no absolute proof of this but it seems probable. So gay males and other groups at risk for AIDS wishing to give "The Gift of Life" NOW HAVE THE RESPONSIBILITY OF MAKING A VERY CAREFUL PERSONAL DECISION BEFORE DONATING BLOOD.

To Help You Decide

- 1 There is no practical test to screen donors' blood for AIDS.
- 2 Although probably very few of us in Manitoba will have the misfortune to get AIDS, the only gay men who can be absolutely certain that their blood might not harm the recipient are those who have been for at least the last 36 months:
 - homosexually inactive
 - involved in an EXCLUSIVELY monogamous relationship with another who has also been monogamous for 36 months.

If in doubt, don't donate. [Emphasis in original.]

The pamphlet was endorsed by Dr Marlis Schroeder, the medical director of the Winnipeg blood centre, who spoke at the forum on behalf of the Red Cross. It was printed in red and white, the colours of the Red Cross. The brochure suggested that gay men whose sexual preference was unknown to colleagues or acquaintances who might accompany them to the blood clinic could telephone the Red Cross after donating and ask that their donation be "used for research purposes only."

Unlike those in most other provinces, AIDS service organizations in Manitoba received financial support from the provincial government during the early 1980s.

Halifax

Dr Robert Frederickson, a family physician in Halifax whose patients included gay and bisexual men, testified that he learned all that he could about AIDS during the early 1980s and routinely passed on that information to his patients in order to minimize the spread of the virus. In June 1983 he learned that, in order to protect the blood supply, gay and bisexual men should be discouraged from donating blood, and from then on he encouraged male patients who engaged in sex with other men not to donate blood, semen, or organs. He also advised any other patient who belonged to a group at high risk of contracting AIDS not to give blood, and spoke to small groups of gay persons on this subject. He began to ask all new patients, as part of their medical histories, when they had last donated blood to the Red Cross.

Other examples

The activities summarized above are examples of the measures taken by gay community organizations, organizations specifically concerned with AIDS, and physicians and other health care workers serving gay patients to educate gay persons at high risk about AIDS and to encourage them not to donate blood. They are not isolated examples. The policy of voluntary self-exclusion was debated actively in *The Body Politic*, the only national gay newspaper of the period. The possibility that AIDS could be transmitted

through blood was reported in *Perceptions*, distributed in Regina and Saskatoon by a health care group called Gay and Lesbian Support Services. *Fineprint*, which served the Edmonton gay community, encouraged gay readers to be responsible sexually and published the Red Cross's request that gay men refrain from donating blood. The newsletter of the Gay Association in Newfoundland published a statement from the organization's executive in early 1983 asking gay and bisexual men not to give blood. Provincial organizations, such as the Gay Alliance for Equity in Nova Scotia, were in contact with the longer-established gay organizations in Toronto. Brochures produced by the AIDS Committee of Toronto were circulated to all regions of Canada and were either reprinted in their entirety or adapted for local publication. In Quebec, some of these brochures were translated into French.

Community efforts of this type played an important role in protecting the blood supply. Where they were early and most extensive, as in Vancouver, the rates of transfusion-associated AIDS were substantially lower than might otherwise have been expected.

July–December 1983: Plans for a pamphlet about AIDS for prospective donors

In the spring and summer of 1983, blood transfusion services throughout the world followed the U.S. lead in telling blood donors about AIDS. The Irish blood transfusion service produced a pamphlet in April 1983 that was modelled after that of the American Red Cross, listing the groups at high risk of contracting AIDS and asking members of those groups not to donate blood. By June, most divisions of the Australian Red Cross were giving donors pamphlets that also followed the American Red Cross model. The Hong Kong Red Cross produced a similar information sheet in June. On 23 June the Council of Europe issued recommendations about AIDS, including one that urged member states to "provide all blood donors with information on the Acquired Immune Deficiency Syndrome so that all those in risk groups will refrain from donating," and appended a copy of the American Red Cross pamphlet. By July 1983, European countries that had not already done so, including France, Belgium, and Germany, began to distribute pamphlets and questionnaires that gave prospective donors information about risk factors for AIDS.

By this time, the Canadian Red Cross was one of the few modern blood transfusion services in the world that was not giving information to prospective donors at blood clinics about the groups at high risk of contracting AIDS and the signs and symptoms of AIDS. Although there were not yet any officially reported cases of transfusion-associated AIDS in Canada, the incidence of AIDS in this country, one of the highest reported incidences in the world, was rising.

The Red Cross sent copies of the Council of Europe's recommendations to its local medical directors for their consideration in July 1983. Some of the local medical directors expressed concern about the current donor-screening

measures. One of them was the medical director of the Regina blood centre. She wrote to Dr Davey in July 1983, suggesting the need for a review of the procedure:

Generally, I think that the current AIDS controversy might serve as a focus for reevaluation of our entire donor screening procedure, for accuracy and thoroughness. A significant number of donors do not read the questionnaire as it exists now. Perhaps the entire donor screening procedure should be reviewed in conjunction with the current review of the Donor Criteria Manual and consideration given to direct (verbal) questioning of the donors re: their health. This would at least ensure that all donors who are accepted would have a 'no' response to the questions at the time of the donation.

Dr Herst, the deputy medical director of the Toronto blood centre, also wrote to Dr Davey, on 22 July, saying that "a clear, up-to-date donor information pamphlet on AIDS is definitely needed." She enclosed a copy of the American Red Cross's pamphlet with suggested revisions to make it more appropriate for Canadian use. Dr Bowen, the medical director of the Calgary blood centre, wrote to Dr Davey on 26 July, recommending that the press releases be supplemented by other means of educating persons at high risk and supporting confidential unit exclusion:

To date, I believe the nationally-waged publicity campaign to inform high risk groups of their social responsibility in not donating blood has been generally successful. We have multiple examples of homosexual or bisexual men with multiple partners informing us that they are voluntarily refraining from donating blood because they are in a "high risk" group. We, therefore, have evidence that most of the people in these high risk groups have a strong social conscience and will refrain from blood donation. However, the information leaflet to be supplied to donors or to be displayed as a large poster at blood donor clinics seems a necessary step to ensure that the majority of members of the high risk groups have indeed been educated as to AIDS ... I am quite interested in the system that John Derrick outlines from the New York Blood Center where the donor is allowed to donate and secretly marks a folded piece of paper as to "please use my blood for research purposes or transfusion." This seems to provide a ready out for people who are reluctant to turn on their heels and leave the clinic without donating blood.

In mid-August 1983, the Red Cross national office was considering whether its efforts to prevent persons at a high risk of contracting AIDS from donating blood ought to be increased or revised. On 18 August, Dr Derrick wrote to Dr Perrault and Dr Davey about issues that needed to be discussed by the

AIDS working group, the committee consisting of Dr Derrick, Dr Davey, Dr Perrault, a number of medical directors, the national coordinator of public relations, and the director of nursing, which had met on 29 March 1983. The issues he raised included the effectiveness of the current program, the merits of providing AIDS-specific information to donors at clinics, and consideration of confidential unit exclusion.

1. In recent weeks we have discussed the continuing developments with reference to AIDS and its possible transmission by blood and blood products. It would seem wise to consider at this time, what, if any, further action should be taken with reference to donor information, donor screening and user information.
2. Among the considerations which would seem to be most pertinent are:
 - a. How effective is the current CRC [Canadian Red Cross] position in discouraging blood donations by members of groups considered to be at high risk of developing AIDS.
 - b. Why are at least some BDR [blood donor recruitment] sectors, and indeed some Blood Donation Clinic staff, in various areas of the country either unwilling or unable to answer donor questions concerning AIDS and the CRC position on acceptable donors.
 - c. Should information be provided at clinics in the form of:
 - i. Posters and pamphlets (e.g. statements by ARC [American Red Cross] and NYBC [New York Blood Center]).
 - ii. Nurses providing information and/or counselling which would help a donor to make up his/her mind to self exclude.
3. Should donors be given the opportunity to "save face" at blood donor clinics by the asking of similar questions (which would be justifiable in view of the current AIDS situation but need not involve direct questions concerning sexual preference, national and/or racial origin, etc.) of all donors and by providing a means of self exclusion such as a confidential sealed form attached to the pack and covering the disposition of their donation either for recipient use or "for research purposes" (i.e. The Greater New York Blood Program approach).

At the same time, another group within the Red Cross, the donor criteria working group, was considering the revision of the donor criteria manual, the reference document used by clinic nurses to determine whether a donor met the criteria for acceptance. The donor criteria manual had not been revised since the late 1970s, and therefore contained no reference to AIDS or its early symptoms or risk groups. The donor criteria working group prepared a list of suggested revisions to the manual in September 1983. One of these was that anyone with symptoms suggestive of AIDS be deferred. Except for the preamble of the questionnaire, which said that the donor should be

"well," the clinics had no material that would elicit information from donors about symptoms of AIDS. The new manual that included deferral of persons with AIDS was not completed until March 1986.

The AIDS working group met on 13 September 1983. Dr Perrault suggested that its terms of reference be amended and that the function of the working group be to advise the national director of the blood transfusion service "in his dealings with Provincial and Federal Committees on AIDS related problems." The working group accepted Dr Perrault's suggestion and changed the terms of reference. No longer did it have any general terms of reference for dealing with the issue of AIDS and blood transfusion.

The working group decided that a more definitive Red Cross position on AIDS was needed and that one should be prepared for Dr Perrault to present to the National Advisory Committee on AIDS at its next meeting. Dr Perrault discussed the "political problems inherent in the Canadian AIDS situation" and said that "the central issue then becomes that of ensuring support from the [National Advisory Committee on AIDS] for the position adopted by the CRC BTS."

The working group decided on a course of action as follows:

- a) Reaffirm high risk groups (ref March 10 statement).
- b) Reaffirm prudence as the basis for current position.
- c) Indicate that no new evidence has been forthcoming to warrant abandoning course of prudence.
- d) Inform [National Advisory Committee on AIDS] of a, b and c and our intent to reaffirm same to BTS/BDR [blood transfusion service/blood donor recruitment] staff.
- e) Inform BTS centres of a-d and outcome.
- f) Inform National Programme Committee Meetings of outcome of a-e.
- g) Inform BTS Advisory Committee on the entire issue and developments.

Dr Perrault told the working group that the blood transfusion service would begin the process of drafting an information pamphlet for use at the clinics. First, a survey would be sent to a number of the centres to ascertain the type of questions that donors had been asking about AIDS. A pamphlet would then be drafted and submitted to the AIDS working group for its consideration. The pamphlet would also be sent to the donor criteria working group, the national public relations department, and the Red Cross's lawyers for their advice and approval.

The National Advisory Committee on AIDS met on 30 September 1983. By this time, the Laboratory Centre for Disease Control had received reports of thirty-nine persons with AIDS in Canada, twenty-two of whom had died. The National Advisory Committee, which included Dr Perrault, endorsed the risk-reduction recommendations that had been published by the Centers for Disease Control in its journal, the *Morbidity and Mortality Weekly Report*,

in March 1983, with the exception of the recommendation that autologous transfusion be encouraged. Two of the recommendations that were thus endorsed were that blood centres should inform potential donors that persons at a high risk of contracting AIDS should not donate blood or plasma and that studies be conducted to determine the effectiveness of surrogate tests for AIDS. The committee did not discuss the specific details of the Red Cross's strategies for donor education. The committee was not told that there were no studies involving surrogate tests being carried out or contemplated.

Dr Derrick prepared a position paper on 26 October 1983 on the status of AIDS and the safety of Red Cross blood and blood products. In it he described the first case in Canada of an infant who had suffered from an AIDS-like condition, but concluded that it was not a case of transfusion-associated AIDS because it did not meet the strict definition of AIDS of the Centers for Disease Control:

The only case of "possibly transfusion associated AIDS" reported to date in Canada has been that of a "white, French Canadian infant who had received two exchange transfusions at birth for ABO incompatibility" reported in the September 1 issue of the *NEJM* [*New England Journal of Medicine*] by Norman Lapointe, M.D. and colleagues at Hôpital Sainte Justine, Montreal. However, given Dr Evatt's observation that CDC [Centers for Disease Control] is currently not classifying children as AIDS patients "*because current knowledge does not provide adequate definition of what is or is not normal immune function in very young children,*" it must be concluded that, with Canadian authorities' acceptance of the CDC definition of AIDS, and therefore of this classification, there have been no incidents of transfusion associated with AIDS cases reported in Canada to date. [Emphasis in original.]

Dr Derrick wrote in the position paper that the Red Cross's position on donor deferral was "essentially unchanged in its commitment to voluntary self exclusion by blood donors who may be members of 'high risk groups.'" He said that this position had been unanimously endorsed by the medical directors, the blood transfusion service advisory committee, and the National Task Force on AIDS (the precursor to the National Advisory Committee on AIDS), but that it had been criticized by other persons for its identification of recent Haitian immigrants as a high-risk group and for its failure to question potential donors directly as to whether they belonged to a high-risk group. Dr Derrick said that more "aggressive" screening measures taken by U.S. health authorities had been "taken in response to the pressures exerted by the media, user groups and other special interest groups on the various governmental, commercial and voluntary agencies involved in the collection, processing and distribution of blood and its products."

In his position paper, Dr Derrick emphasized that the incidence of transfusion-associated AIDS was very low and that therefore the Red Cross would not expand its donor deferral policy beyond that of voluntary self-exclusion:

In the intervening six to eight months since the inception in the U.S. of expanded medical screening for signs and symptoms of AIDS, it has become apparent that while indeed the agent responsible for the syndrome probably is blood borne, the incidence of AIDS developing as a result of blood transfusion is extremely low. As noted in Item 1, there have been at most 15 cases of AIDS reported in which blood transfusion is suspect. This, on the basis of 10 million transfusions carried out in the U.S. over the last three years works out to 1.5 in a million chances of developing AIDS from blood transfusion in a country in which the syndrome is five times as prevalent as it is in Canada.

Given those odds, the Canadian Red Cross has chosen not to expand its medical screening of blood donors beyond voluntary self exclusion until such time as there are firmer indications to do so. The experience in the United States with reference to the effects of the more aggressive screening of donors on the blood supply has been variable. For the New York Blood Center, it has meant the removal of three percent of donated units from the system and a decrease of twelve percent in male donors between the ages of 24 and 36. On the other hand, an American Association of Blood Banks survey of some 135 facilities nation-wide, revealed few AIDS-related collection problems.

He also said that the Red Cross had plans for the "early preparation of a pamphlet" that would include an appeal to persons at a high risk of contracting AIDS to exclude themselves.

The position paper was presented to the National Advisory Committee on AIDS when it met on 9 November 1983. At that meeting, Dr Perrault said that the Red Cross was "unwilling to change its present screening procedures unless more cases of AIDS related to blood transfusion became apparent." The position paper was also given to the blood transfusion service advisory committee on 18 November. That committee formally endorsed the Red Cross's position on screening:

[B]ased on the current evidence and knowledge with reference to the extremely small risk of acquiring AIDS through blood transfusion, or other therapy utilizing blood components or plasma derivatives, as compared to the beneficial effects therefrom, the Canadian Red Cross will continue its present course of appealing to well-informed, and, by virtue of the fact that

they are voluntary, well-motivated donors to self-exclude from donating blood where there is any possibility that their donation might harm rather than help a recipient.

By this time, the Laboratory Centre for Disease Control had received reports of fifty persons suffering from AIDS in Canada, twice the number that had been reported by May 1983, six months earlier. Of the fifty persons, half had died.

In mid-November, an AIDS pamphlet was being prepared by Dr Derrick, Mary-Ann Lark, the national director of nursing, Eva Bart, the national coordinator of public relations, and Ron Rea, the national coordinator of blood donor recruitment. These persons constituted the Canadian Red Cross national office ad hoc working group on AIDS.

By this time, the Red Cross AIDS working group that had met on two occasions no longer existed and its functions had been assumed by the immunology-virology working group. That group met on 23 November. The Red Cross continued to be highly sceptical of the evidence of the transmission of AIDS by transfusion. Dr Derrick told the meeting:

The CRC [Canadian Red Cross] has chosen not to expand its medical screening of blood donors beyond voluntary self exclusion until such time that there may be firmer indication to do so. The incidence of AIDS cases in Canada is $\frac{1}{5}$ that in the U.S., the number of hemophiliacs with AIDS has not increased in the last 6 months, and none of the investigations on possible transfusion related AIDS cases have conclusively identified the transfused blood as the vehicle of transmission.

The same scepticism was apparent in a memorandum from Dr Derrick to the local medical directors dated 20 December 1983. Attached to the memorandum was his position paper of 26 October 1983. Dr Derrick wrote:

On the basis of the evidence to date it seems probable that the agent(s) responsible for the development of AIDS is probably blood borne, or that the blood is an optimal portal of entry. The danger and/or incidence of AIDS developing as an outcome of transfusion of blood or blood components would appear to be minuscule, however. Further, insofar as plasma derivatives are concerned, only the coagulation preparations Factor VIII and IX are suspect as possible causative factors in the development of AIDS in hemophilia patients. The syndrome developing in hemophiliacs has several basic differences from that observed in the other groups especially affected by AIDS.

The current position of CRC [Canadian Red Cross] on Donor Screening is based on those developments, and the fact that AIDS does not yet appear to be developing in Canada in the exponential manner seen in the U.S. There are many now who consider that the importance of AIDS as a threat to public health in this country has been overrated.

In the memorandum, Dr Derrick told the medical directors that the Red Cross's position paper had been, "with the exception of a minor wording change, accepted in totality" by the National Advisory Committee on AIDS and had been "supported unanimously" by the members of the national blood transfusion service advisory committee. In fact, the Red Cross's position paper had not been endorsed by the National Advisory Committee on AIDS. It had not been the subject of comment, either positive or negative, by that committee. He attached to his memorandum a "mock up" of the pamphlet that had been prepared in mid-November.

January 1984: Confirmation of the link between transfusion and AIDS

On 4 January 1984, the *New England Journal of Medicine* published a report of a study by Dr James Curran and colleagues at the Centers for Disease Control of eighteen cases of suspected transfusion-associated AIDS. None of the recipients possessed any risk factor other than the receipt of blood components. The investigators of the study concluded that blood components could transmit AIDS, that exposure to only one infected unit might result in transmission, and that donors who had developed no symptoms of AIDS could be infectious.

The information reported in the article was widely known months before it was published in the journal. Dr Thomas Zuck, an eminent U.S. blood banker and the director of the division of blood and blood products of the U.S. Food and Drug Administration between 1985 and 1987, said that the effect of the study was to "put the whole medical community and perhaps the world on notice that AIDS is transmitted by blood transfusions, period."

Dr Davey did not agree with Dr Zuck and most of the U.S. blood bankers who regarded the Curran article as bringing an end to any reasonable question about the existence of transfusion-associated AIDS. He testified that he had interpreted this study "only as a statement that increased the odds considerably."

To coincide with the publication of the report in the *New England Journal of Medicine*, a joint statement about AIDS was issued by the American Red Cross, the Council of Community Blood Centers, and the American Association of Blood Banks. It included recommendations for action by their members. One of these was that interviews at clinics be arranged to make it possible for donors in high-risk groups to refrain voluntarily and confidentially from donating. Another was that donors in areas of high incidence of AIDS be given

a means to indicate discreetly at the time of donation or soon thereafter that their donations should not be used for transfusion. The American Red Cross accomplished this quite simply by adding the following statement to its information pamphlet about AIDS:

If you donate blood today and have any additional questions or concerns about whether your blood should be used for transfusion, please call the blood center as soon as possible.

The American Red Cross told its centres on 3 January 1984 that the revised information pamphlet being prepared in anticipation of the report in the *New England Journal of Medicine* would be available for distribution on 16 January and would be in full use by 1 February.

The new American Red Cross pamphlet also contained a revised definition of risk groups:

- Persons with symptoms and signs suggestive of AIDS. These include severe night sweats, unexplained fevers, unexpected weight loss, lymphadenopathy (swollen glands) or Kaposi's Sarcoma (a rare cancer).
- Sexually active homosexual or bisexual men with multiple partners (more than one).
- Recent Haitian entrants into the United States.
- Present or past abusers of intravenous drugs.
- Sexual partners of persons at increased risk of AIDS.

The definition of "multiple partners," which had been a source of confusion, was now clarified to mean "more than one." This recognition of the risk of AIDS from a single homosexual contact was consistent with the comments made by Dr Herst at the July 1983 press conference in Toronto.

January–May 1984: Publication of the Canadian Red Cross AIDS information pamphlet

On 10 February 1984, Dr Derrick reported to the administrative working group of the Canadian Red Cross, an executive committee of medical directors representing different geographic regions of Canada, that a draft of the donor information pamphlet had been completed. It was being submitted to the donor criteria working group, which was to comment by 1 March. Four days later he sent the draft of the pamphlet to the chair of the donor criteria working group, Dr Gorelick, the medical director of the Halifax blood centre, with the following message:

With our particular awareness here at the National Office of the strong pressures on the Canadian Red Cross for more definitive action with reference to donor screening and the problem of AIDS, it has been the goal of

the Ad Hoc group associated with development of the donor information pamphlet to react to the mandate of the BTS [blood transfusion service] Advisory Committee as responsibly and quickly as possible. Dr Perrault and Dr Davey are asking that any residual problems concerning implementation of the pamphlet be cleared up with all possible speed in view of the imminence of both the Medical Directors Meeting and that of the BTS National Advisory Committee. It would be very much appreciated, therefore, if the matter of text approval, and any related issues with reference to implementation of the pamphlet, be taken up by the Donor Criteria Working Group with all possible speed. In view of her active participation both in the group and in the Ad Hoc group responsible for the development of the pamphlet, it is suggested that Mrs Lark [the national director of nursing] be designated as the liaison person between the two groups.

Dr Perrault has indicated that he is expecting to be able to report full implementation of the AIDS information mandate at the April 26th meeting of the BTS Advisory Committee. To meet this deadline, given a minimum production time of six weeks from the day of approval of the final text, (as quoted by Mrs. Bart [the national coordinator of public relations]), comments and suggestions from your Working Group will have to be available for incorporation and finalizing no later than March 1.

Dr Gorelick responded in a telephone conversation on 1 March. He suggested that, since information about the risk of AIDS was quickly changing, the print run of the pamphlet should be small so that the Red Cross would not be left with obsolete copies. He also suggested that the introduction of the pamphlet be carefully monitored to record any difficulties experienced in the various centres and that it be possible to revise the pamphlet in accordance with new information in the future.

The national office decided to print 250,000 pamphlets, which represented approximately a three-month supply at the rate of one pamphlet per donor. It aimed to start distributing the pamphlets at the end of April.

By March 1984, many more cases of transfusion-associated AIDS had been identified in the United States. When the National Advisory Committee on AIDS met in Ottawa on 20 March, Dr James Allen of the U.S. Centers for Disease Control was present. The minutes record his report:

In the US, 37 adults and 7 or 8 children had been identified who received blood transfusion within five years of the onset of AIDS. In the majority of these cases, no other risk factors were apparent, and a search for other possible means of transmission had been sought. So far, only one infant and one adult had developed transfusion-associated AIDS where a member of the donor pool had also developed AIDS. He indicated that the problem of blood donation by asymptomatic individuals prior to the onset of AIDS being identified required further and continuing study.

By the date of the National Advisory Committee meeting, seventy-two Canadian cases of AIDS had been reported to the Laboratory Centre for Disease Control. The epidemic in Canada was still one and a half years behind that in the United States; that is, in March 1984, the prevalence of AIDS in the Canadian population was similar to that in the U.S. population in the autumn of 1982. Unless measures were taken to reduce the spread of AIDS in Canada, it could be expected that it would continue at the same rate that it had in the United States.

During the same month, March 1984, the *Canada Diseases Weekly Report* published the contents of an information document about AIDS that had been prepared for health care workers by the National Advisory Committee on AIDS. It included a section prepared by the Red Cross concerning the risk of AIDS from blood and blood products. The Red Cross did not reveal that, after exchange transfusions, an infant in Quebec had developed a condition that was associated with AIDS. It again minimized the risk of transfusion-associated AIDS:

Current indications are that the probability of developing AIDS following blood transfusion is very low. In the U.S., based on the estimated number of transfusions and the number of "transfusion-associated AIDS cases" reported during the last five years, the chances of developing AIDS from blood transfusion are approximately 2 in a million. In Canada, no cases of AIDS have been linked to blood transfusion. There is currently no available evidence that blood transfusion recipients are at higher risk of developing AIDS. Nevertheless, the possibility that AIDS can be transmitted in this way cannot be dismissed. The prolonged incubation period increases the possibility of transfusion-related cases being identified in the coming years.

The Red Cross local medical directors met on 29 and 30 March 1984. Dr Derrick told them that the blood transfusion service was "putting forward a strong information campaign to have well informed donors and recipients" and that new donor information would soon be available. Concern was expressed that giving donors the pamphlets would prolong the donation process. A representative of the American Red Cross, who attended the meeting as a guest, said that the experience in his region, Massachusetts and Maine, was that the pamphlet did not interfere with the donation process.

On 1 May 1984, the Red Cross pamphlet, *An Important Message to Our Donors*, which had been completed two weeks earlier, began to be used in Red Cross blood centres. Every centre was given a three-month supply and instructed to give the pamphlet to prospective donors as part of the pre-donation procedure. The medical directors were instructed to complete a questionnaire about the use of the pamphlet at their centres; the responses to it of donors, staff,

and volunteers; and any problems that had been encountered. That questionnaire, to be completed after the pamphlet had been used for six weeks, was to be submitted to the national office by 29 June.

The entire text of the pamphlet read as follows:

WELCOME

The Canadian Red Cross thanks you for volunteering to be a blood donor. Your donation can be made without risk to your own health. However, in order to ensure that your well being, and that of those who will receive your generous gift are maximally protected, before donating you should:

- Be sure that you are feeling generally well.
- Study the donor questionnaire on the reverse side.
- Consider the following information carefully.

There are a few illnesses which can be transmitted from donors to recipients and, should there be any indication that such an illness is a possibility it may be necessary, temporarily at least, to exclude from donation. This is because some apparently healthy persons can carry viruses or other agents in their blood which, while not necessarily harmful to themselves, may result in illness in the recipient of their blood. Among these infective agents are hepatitis, yellow fever, malaria and possibly other more unusual diseases occurring in other parts of the world. This is the reason for the inclusion in the donor questionnaire of questions related to these illnesses and to practices and travel which could possibly result in their development.

Recently it has become apparent that the condition known as AIDS (Acquired Immune Deficiency Syndrome) is probably blood borne and should be included in the list of illnesses which excludes donation.

AIDS is a condition in which the body's natural resistance to various diseases is seriously reduced, frequently with fatal results. The cause is unknown. There is no laboratory test to detect it in its early, non-symptomatic stage. Therefore, it is recommended that for the present, persons who have been indicated, according to current evidence, as being at above average risk of contracting AIDS should not donate blood.

These persons include:

- homosexual or bisexual males who have multiple partners
- present or past abusers of intravenous drugs
- recent immigrants from, or visitors to, those areas where AIDS is endemic, i.e. Chad, Haiti and Zaire
- sexual partners of any of the above persons

If, after reading this pamphlet and the questionnaire, you feel you should not donate blood at this time you may indicate this to the nurse. **There is no obligation to identify your reason(s) for not donating.**

Should you have further questions, the clinic nurse or the Centre Medical Director will be more than happy to answer them.

Thank you very much for coming and for giving us your attention and cooperation. [Emphasis in original.]

Unlike the American Red Cross's pamphlet produced in January 1984, the Canadian Red Cross's pamphlet did not define "multiple partners," nor did it include persons with symptoms of AIDS in the groups of persons who should not donate blood. There was no requirement that donors acknowledge that they had read the pamphlet, either by signing the pamphlet or by being interviewed by a nurse. There was no statement at the end asking donors to call the blood centre after donating if they believed that their donations should not be used for transfusion.

July–December 1984: Evaluation and continuation of the AIDS pamphlet pilot project

The questionnaire sent to the medical directors was prepared by the Red Cross public relations department and had three parts. The first two related to the manner of distribution and the number of blood donors reached. The third part dealt with the reaction of blood donors to the pamphlet. The public relations department suggested various ways of evaluating the pamphlet, including "focus groups" and in-depth interviews. Focus groups would have involved intensive interviews with groups in order to determine their responses to the pamphlet, including the effectiveness of the communication and whether they were offended by it. No centres convened focus groups to evaluate the pamphlet.

Some centres had responded to the questionnaire by the end of July. They described a variety of practices in distributing the pamphlet. There was a common concern that donors were not reading the pamphlet thoroughly, because of a lack of interest or a lack of time. The Halifax centre reported that donors read the pamphlets "at their leisure or not at all." The Ottawa blood centre reported that "as with the questionnaire, regular donors do not read the pamphlet attentively before donating." In Sudbury, most donors were not reading the pamphlet, or were reading only part of it. In Saskatoon, many pamphlets were found lying around the clinic area. Some centres reported that they were not handing the pamphlets out before donation as they had been instructed to do. In Sudbury, donors received the pamphlet after they had finished giving blood. In Edmonton, donors were given the pamphlets while they were donating. Other centres were uncertain whether the pamphlet was supposed to replace the donor questionnaire. No centre reported that donors were offended by the pamphlet.

The language in the pamphlet reflected the literacy level of a person with a grade 10 education. As a result, the pamphlet would not have been understandable to a significant proportion of the general population, approximately

16 per cent of whom, according to a Statistics Canada report in 1989, possessed reading skills too limited to allow them to deal with the majority of written material encountered in everyday life. The level of the pamphlet was considerably higher than that. It had never been tested on a sample of donors to determine whether its meaning could be readily understood.

Although pamphlets had been prepared in both English and French, allocation to the various centres was not always sufficient. The delivery of French-language pamphlets to Ottawa, where a significant number of donors were French-speaking, was delayed. Only 2,000 English-language pamphlets were given to the Montreal centre (as opposed to 30,000 pamphlets in French); the same number was sent to Quebec City, which had a much smaller English-speaking population.

By July 1984, ninety-six Canadian cases of AIDS had been reported to the Laboratory Centre for Disease Control. The fatality rate was 57 per cent and the latency period was now believed to be as long as three years.

The pamphlet program had been implemented as a three-month pilot project, with a three-month supply of pamphlets. By mid-August, only 4,000 copies remained at the national office. At the end of the three months, after the evaluations were received, and despite the problems revealed by them, there was no formal review of the program.

On 19 September 1984, a person who had contracted AIDS as a result of a blood transfusion in the United States was reported to have started a civil action for damages against the blood centre that had collected the blood. This news item prompted Dr Perrault to request a report on the status of the pamphlet program. Dr Derrick prepared a briefing paper for the blood transfusion service advisory committee. That paper summarized the responses to the evaluation, but noted that the level of response had been too small to provide sufficient data for an accurate assessment. He recommended that the use of the donor information pamphlet be extended for three months, and that the evaluations be modified so that the responses could be more readily processed and analysed. He recommended that staff of the blood transfusion service and blood donor recruitment program be told that the use of the pamphlet was obligatory.

By the end of September there were 117 cases of AIDS in Canada. They included seven pediatric cases that were, by this time, being counted. The fatality rate was still more than 50 per cent. In addition, another case of transfusion-associated AIDS in Canada, the first in an adult, had appeared. It was well known but had not been "officially reported" because it had occurred in Quebec, a province in which AIDS was not reportable at the time.

By late October 1984, there had not been any direction from the national office to the medical directors with respect to the continuation of the pamphlet program. By then there were 131 cases of AIDS in Canada. Seventy-four cases of transfusion-associated AIDS had been reported in the United States.

Dr Bowen, the medical director of the Calgary blood centre, wrote to Dr Davey on 26 October 1984 to express his concern about the donor education program:

I am concerned that the donor brochure produced in response to the AIDS issue has gone out of print, without apparent direction as to what action to take as a National Transfusion Service, in response to the AIDS issue and donor deferral. It alarms me that perhaps no uniform approach is being taken at centres regarding education of the public, "regarding high risk groups," [and] the education/informing of blood donors at donor clinics [by] requesting that donors from high risk groups continue to voluntarily refrain from blood donation. Thus it is difficult to state, as a Medical Director, that the CRC BTS [Canadian Red Cross blood transfusion service] has indeed responded to the AIDS concern with a uniform approach of public education and ensuring donor awareness at the clinics with a standardized information transmissal system such as the brochure that was in use. Are all the centres using the brochure?

The blood transfusion service advisory committee met on 2 November 1984. The minutes state the following:

Dr Derrick and Mrs Bart [the coordinator of public relations] reported on the use of and reaction of donors to the pamphlet on AIDS. Preliminary results indicate a disappointing lack of response to the questionnaire which had been designed to test the effectiveness of the pamphlet. Renewed efforts will be put into redesigning the questionnaire and stressing the importance of the use of pamphlets to B.D.R. [blood donor recruitment] and Medical Directors' Administrative Working Group.

Dr Davey responded to Dr Bowen's letter on 6 November 1984. He wrote:

The donor brochure on AIDS is to continue in use. Laminated reusable copies of the present text will be available shortly, for use until a revised brochure is produced: the revision is in hand.

The BTS Advisory Committee on 02 Nov '84 stated that to inform donors about AIDS is not an option but an obligation, and all Centres are to be informed of this resolution. Self-exclusion is recognized as the most effective form of prevention at present.

On 22 November, Dr Perrault asked the national office ad hoc working group on AIDS (Dr Derrick; Mrs Lark, the national director of nursing; Mrs Bart, the national coordinator of public relations; and Mr Rea, the national coordinator of blood donor recruitment) to meet to consider the modification

of the pamphlet and the redesign of the questionnaire. He also asked them to consider how the ad hoc working group and blood donor criteria working group could work together to improve the pamphlet.

The ad hoc working group met on 13 December and decided to continue the distribution of the pamphlet "on an extended pilot basis" until April 1985. No changes to the text or the format would be made during the pilot project. Mrs Lark and Mr Rea were given the task of determining the inventory of pamphlets at each of the blood centres. Mr Rea reported on 19 December that the blood centres at Calgary, Saskatoon, and Halifax required additional paper pamphlets and that the blood centres at Calgary, Saskatoon, Edmonton, and Regina required additional laminated pamphlets. Mr Rea said that it appeared that the Montreal and Saint John blood centres were "not using the pamphlet."

January–May 1985: Concerns about use of the pamphlets

On 9 January 1985, Mrs Lark reported about the inventory of pamphlets in the blood centres to Dr Davey. She concluded:

1. Overwhelming evidence is provided by the attached forms that this pamphlet is not being used as instructed by yourself and Dr Perrault as a specific screening tool for AIDS at clinics.
2. Dr Derrick has shared his profound concerns of our culpability when (not if) Canadian doctors identify transfusion related cases of AIDS. Current data supports these concerns.
3. The attached copy from the January 9th *Globe and Mail* indicates we are routinely screening for AIDS. I believe this would be difficult to prove.
4. I propose we initiate an immediate rewrite of the Donor Questionnaire and include all pertinent questions regarding AIDS risks.
5. It is my conviction that we must be seen to be, and must be, protecting the recipient population.
6. The pamphlet can be used as an information tool at clinics and by BDR [blood donor recruitment] but by strengthening our questionnaire we will strengthen our position on this urgent issue.
7. For discussion with the writer and all recipients of this memo at the earliest convenience.

Dr Derrick expressed a similar concern the next week in a memorandum to Dr Perrault and Dr Davey. He wrote:

For several months now Mrs Lark, Mr Rea and I have been very concerned with the apparent apathy of a significant proportion of CRCS [Canadian Red Cross Society] Blood Programme staff toward use of the Blood Donor Information Pamphlet.

... it is apparent from the survey carried out by Mr Rea, and from information I have received personally from media reporters testing our system of donor screening, that some areas of the country are not using the pamphlets at all ...

While it is true there are no cases of AIDS in Canada which can be attributed strictly to transfusion, it is certain that this will occur eventually, possibly soon, and unless the CRC is seen to be exerting every effort to screen out high risk donors when this does happen, the credibility of the Blood Transfusion Service will be badly damaged.

By the beginning of 1985, it was possible to test for the presence in blood samples of antibody to HIV, and alarming evidence was emerging about the extent to which the virus had spread in high-risk groups. The data from several studies carried out in the United States were published in the *Morbidity and Mortality Weekly Report* on 11 January 1985. Depending on the study, between 22 and 65 per cent of homosexual men tested were found to be HIV-antibody positive, as were 87 per cent of intravenous drug abusers and 56 to 72 per cent of persons with type A hemophilia. HIV had been isolated from 85 per cent or more of the persons found to be HIV-antibody positive. The studies also revealed that the virus could remain in the bloodstream in infected persons, even if they developed no symptoms. Studies in Canada showed that a high proportion of severe hemophiliacs, and a significant proportion of homosexual men, were infected with HIV. The significance of these data, for those concerned with the safety of the blood supply, was that a large proportion of persons in groups at high risk of contracting AIDS were infected with HIV and were themselves infectious, but many of them would not have any symptoms of AIDS and would feel well enough to donate blood. These data underlined the need to communicate effectively with members of high-risk groups and persuade them not to donate blood.

At the end of January 1985, the board of directors of the Red Cross expressed concern about failures in the distribution of the society's AIDS information pamphlets. The minutes record the following comments by Andrew Fleming, the vice-president:

Mr Fleming brought to the attention of the meeting the fact that some centres/clinics were apparently not distributing to blood donors the pamphlet which had been prepared as a result of the AIDS situation. He noted the responsibility which might be incurred by the Society's directors and officers should this situation continue. The Secretary General stated that he would investigate the matter, have it rectified where required and report back to the Executive Committee.

The board's concern was conveyed to Dr Perrault and Dr Davey.

On 13 February 1985, the Red Cross learned that a two-and-a-half-year-old Canadian boy with hemophilia, who had been treated only with cryoprecipitate, had been found to be HIV-antibody positive.

Dr Perrault reported to the secretary general on 19 February that the "pamphlet pilot run had not been successful" and that the information given to donors had to be reviewed. He said that other procedures, such as the confidential unit exclusion program developed by the New York Blood Center, ought to be examined. He said that a revised draft of the pamphlet was being prepared and was expected to be approved by the blood transfusion service advisory committee in April.

On 27 February, Janet Wells, the acting area manager of the blood donor recruitment program in Toronto, reported to Linda Larmour, the assistant nursing supervisor at the Toronto centre, that she had learned that the pamphlet was "being used less and less," and that a laminated health questionnaire was "used either instead of, or as well as the pamphlet." The health questionnaire still contained no mention of AIDS, or of its symptoms or precursor states, or of the groups at high risk of contracting AIDS. It was not a substitute for the AIDS pamphlet. Ms Larmour responded on 26 March, outlining the procedure in the Toronto centre for providing pamphlets to donors. She noted that

[t]here was a brief period earlier this year when the pamphlets were out of stock nationally which may have led to the impression that they were no longer required.

The pamphlet and the laminated questionnaire serve different purposes.

During a meeting of the medical directors on 27 and 28 March, Dr Derrick said that "the dikes are breaking" and there might soon be cases of transfusion-associated AIDS in Canada. Dr Perrault said that there would be "an issue of liability" if donor-screening practices were not followed. Another Red Cross official suggested that the most acute problem in the donor information program was that of volunteers who could not be forced to follow policy. After the meeting, Dr Davey wrote to the medical directors to stress the importance of using the pamphlet:

During the AIDS discussion at the Medical Directors meeting, it was evident that all Centres are not using the pamphlet "An Important Message to Our Blood Donors" at all clinics.

Would you please ensure that each donor is being asked to read this pamphlet before donating blood. Failure to do so will be a liability to the Society should any case of transfusion-associated AIDS occur.

A few weeks earlier, on 7 March 1985, Dr Davey had attended a meeting of a task force of the National Advisory Committee on AIDS, called to discuss issues related to the implementation of testing for HIV antibody in donated blood. He reported that Red Cross donor-screening policies had "not had a major effect on the number of blood donors and, although unable to systematically evaluate its effectiveness, the general impression was that the system [was] effective."

Despite the thorough and contemporaneous documentary records suggesting that pamphlets were not universally and consistently distributed throughout Canada, the medical directors and other Red Cross employees who testified about the issue of distribution of pamphlets said that pamphlets were in full distribution at all times in their blood centres. Two explanations were given of how a three-month supply of pamphlets could last for eight months or longer. The first was that many pamphlets were not taken away by the donors and were reused. This explanation is implausible. For example, the Saint John blood centre was sent 5,000 pamphlets. Approximately 40,000 donations were collected at that centre annually. In eight months, assuming an even flow throughout the year, the centre would have processed nearly 27,000 donations. According to Vincent Veinotte, the director of the donor recruitment department of the Red Cross's New Brunswick division, some pamphlets were recovered and used again, but some were taken away by donors and not reused. It is therefore improbable, as Mr Veinotte agreed, that a diminishing supply of 5,000 pamphlets would have been sufficient for 27,000 donations if every donor had been given a copy each time he or she gave blood. The second explanation was that pamphlets were laminated and then reused. In mid-August of 1984, Mrs Lark had suggested that a thousand pamphlets be laminated and distributed to the centres. Although there is evidence that the Red Cross did laminate some pamphlets, this was not done until after November 1984, more than six months into the pilot project.

Some blood centres used other methods to communicate with donors. Dr Gail Rock, the medical director of the Ottawa blood centre, enlarged a copy of the first Red Cross press release soon after it was issued in March 1983 and posted it, in both languages, at permanent and mobile clinics in Ottawa. The press release was also laminated and posted in Quebec City clinics. Dr Jean-Michel Turc, the medical director of the Edmonton blood centre, reported that his centre had prepared an AIDS poster that listed groups of people at high risk of contracting AIDS. Between 20 March 1985, when it was first displayed, and mid-May 1985, three donors decided to exclude themselves. Each of these persons had previously donated, even after the pamphlet began to be distributed in April 1984. Dr Turc concluded that the poster was more effective than the pamphlet in communicating with donors about AIDS. He told the national office about this poster in mid-May 1985, but it did not become part of the national program.

On 14 May 1985, a meeting was held at the national office to discuss the development of a program similar to the confidential unit exclusion program used at the New York Blood Center. The reason for the meeting was that Dr Derrick had received reports that some members of high-risk groups were continuing to donate blood.

August 1985–November 1986: Revised Red Cross pamphlets

By the summer of 1985, the senior Red Cross officials still did not appreciate the serious threat that AIDS posed to the blood supply. On 4 July 1985, Dr Davey attended a federal-provincial meeting in Ottawa about AIDS. He spoke about the significance of testing blood for HIV antibody as a measure to protect the blood supply:

Had this type of testing been available to the CRCS [Canadian Red Cross Society] in the past 5 years, only three cases of AIDS would have been prevented at this point in time. Future activities of this type by the CRCS may reduce the numbers of AIDS cases reported by the order of only 1–2%.

The Red Cross pamphlet was redrafted during the summer of 1985, and the new version was sent to blood centres at the end of August. By that time the Canadian Blood Committee had approved funding for testing all donated blood for HIV antibody, and the Red Cross was preparing to implement testing. More is said about that subject in Chapter 12. The description of risk groups in the new pamphlet had been changed to:

- Active homosexual or bisexual males.
- Drug abusers, both men and women, who inject drugs.
- People who have been to areas during the last 5 years where AIDS is endemic, for example Chad, Haiti, Zaire.
- Sexual partners of people of the above groups.

This pamphlet, like its predecessor, did not tell donors who might be concerned about the safety of their donations to communicate with a representative of the blood centre after giving blood. It did not make any reference to the symptoms of AIDS, nor did it accurately describe the behaviour that put persons (specifically homosexual men) at risk of contracting AIDS. At that time, the definition of risk for homosexual men used in the United States was “any male who had sex with another male since 1977.” Dr Noel Buskard, the medical director of the Vancouver blood centre, introduced his own pamphlet in November 1985, using that definition. Although he had no authority to depart from the national procedure, he did so because he thought his pamphlet was better. It was a better pamphlet.

In January 1986, the Red Cross revised its pamphlet to define as at high risk "any male who has had sex with another male since 1977." It also included the symptoms of AIDS. Dr Derrick notified the medical directors that the new pamphlet would be available after 24 January. He said that the old pamphlet was "seriously outdated" and that any remaining copies were to be destroyed upon receipt of the new one. In November of that year, the Red Cross again revised its pamphlet and for the first time included a notice that persons who did not believe that their donations should be used for transfusion could notify the blood centre of this fact.

Effectiveness and eventual implementation of confidential unit exclusion

Confidential unit exclusion, which had been developed by the New York Blood Center in early 1983, was not used in Canada for another two and a half years, and then only in a pilot project. It did not become available throughout the country until the autumn of 1988.

Confidential unit exclusion gave donors an opportunity to indicate privately that their donations should not be used for transfusion; it thus compensated for the lack of privacy at most blood clinics. In the autumn of 1985, the Red Cross began at its Toronto centre a study of confidential unit exclusion that continued until the following May.

By that time the Red Cross had begun testing all blood donations for the presence of HIV antibody. Even so, there was still good reason to give high-risk donors a means of excluding themselves or their donations without embarrassment. The two tests used for the detection of HIV antibody were the initial screening test, known as ELISA (enzyme-linked immunosorbent assay), and the more accurate, more difficult, and more expensive western blot test. (Both are described in Chapter 12.) After November 1985, all blood donations in Canada were ELISA tested, and those that reacted positively were confirmed by the western blot test. Not all donations infected with HIV can be detected by the ELISA test, however. In particular, the test cannot identify antibody from recently infected donors who are in the "window period," during which they have not yet developed enough antibodies to HIV to trigger a reaction.

The continuing importance of confidential unit exclusion was demonstrated during the study of its use in Toronto. One donation, which its donor had designated should not be used for transfusions, did not react to the ELISA test but was positive according to the western blot test. If it had not been for confidential unit exclusion, that donation probably would have been used for transfusion.

In the study, donors were given the opportunity to designate that their blood should not be used for transfusions but could be used for laboratory purposes. A small proportion of all donors, less than 1 per cent, designated their donation "for laboratory purposes" or failed to fill out the form. Those

who had designated that their donations should be used for laboratory purposes had a much higher prevalence of HIV and of non-A, non-B hepatitis than those who did not designate their donations for laboratory purposes. Donors who designated that their donations should be used for laboratory purposes were also ten times more likely to be confirmed as being HIV-antibody positive, according to the western blot test, than persons in a control group representing the same age, sex, and clinic site. They were approximately one hundred times more likely to be confirmed as HIV-antibody positive, according to the western blot test, than the general donor population.

Dr Jacob Nusbacher, the medical director of the Canadian Red Cross blood centre in Toronto, described the Toronto study to a meeting of the blood products advisory committee of the U.S. Food and Drug Administration that was held on 11 and 12 September 1986. He reported that the confidential unit exclusion program was "effective and useful in identifying and excluding individuals who may be dangerous donors for diseases other than AIDS." In October 1986, the Food and Drug Administration recommended that the program be implemented throughout the United States.

The Canadian Red Cross took much longer to implement confidential unit exclusion in the blood centres outside Toronto. At a meeting of the medical directors on 28 September 1986, eight of nine medical directors present favoured the implementation of confidential unit exclusion.

In February 1987, Dr Derrick, in a position paper prepared for the medical directors' meeting of March 1987, summarized the state of donor-screening measures in Canada. He described a variety of approaches in different centres:

"Toronto" model: Questionnaire is self-administered; self exclusion [confidential unit exclusion] in effect.

"Calgary" model: A nurse orally reinforces the current questionnaire and answers questions in private. No [confidential unit exclusion].

Current situation in most Centres: Questionnaire is read through and a nurse is available to answer questions. No [confidential unit exclusion].

Several other Centres are considering or putting into effect increased screening procedures at donor clinics.

Dr Derrick said that the variety of measures had implications for the Red Cross's liability in the event of any infection of recipients of blood, blood components, or blood products:

Inadequate screening may allow donors to [donate] units that may be potentially dangerous to recipients.

The Red Cross has the obligation to put all reasonable procedures into effect to prevent transfusion associated disease.

In addition the Red Cross must be seen to be effectively screening donors and must be able to establish beyond reasonable doubt that these procedures have been followed in any particular case.

If the Red Cross cannot establish that it has taken all practical measures to prevent transfusion associated disease it may be liable for transmission of the disease and the consequences.

He recommended that a survey be conducted of Red Cross blood centres to determine what kind of donor-screening measures were being done and that minimum screening procedures be established.

Marilyn Harbottle, who was now the Red Cross's national director of nursing, reported the results of the survey of blood centres' donor-screening measures at a meeting of the medical directors in November 1987. The results were summarized in a position paper:

CURRENT SITUATION

Screening procedures across the country are inconsistent and in some areas ineffective, giving mixed messages to donors and the public as to our commitment to provide a safe blood supply.

Laboratory testing of blood does not detect antibodies to the AIDS virus during an undetermined "window" period. Recent recall of factor VIII and IX produced in 1986 indicate that testing and heat treatment may not be effective, therefore, donors must be more intensely screened prior to collection.

American standards for screening are more thorough than those of the CRCS [Canadian Red Cross Society]. Cutter inspectors [from Cutter Laboratories Inc., a major U.S. fractionator supplying blood products to the Red Cross] have expressed concern that our screening does not meet FDA [U.S. Food and Drug Administration] regulations as required for other plasma collection centres.

Current screening guidelines do not:

- a) allow for private questioning of donors;
- b) require proof of donor identity;
- c) provide a record of donor acceptance/deferral; and,
- d) provide a record of who performed the various functions involved in processing the donation.

Due to the excessive amount of screening material which donors are requested to read, they have become complacent, further compromising the effectiveness of this screening method.

There is resistance to the idea of a more thorough screening procedure based on the perception that donors will object and that the longer process will discourage donors from returning.

Ms Harbottle recommended a series of enhanced screening measures, including confidential unit exclusion in places "where the incidence of transmissible diseases is higher than the national average."

During the next several months, new screening measures were developed. These included more detailed interviews with donors, conducted by nurses, about their medical history and current health, and a revised questionnaire that included AIDS-related questions. Eventually, confidential unit exclusion was implemented throughout Canada in the autumn of 1988, two years after Dr Nusbacher's study was published.

Other risk-reduction measures

Other measures to reduce the risk of contamination of the blood supply by the causative agent of AIDS had been contemplated as early as January 1983, but were not instituted until the late 1980s – or at all. The joint statement of the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers, issued on 13 January 1983, had set out a number of measures aimed at reducing the risk of AIDS from blood transfusion. They included the promotion of autologous transfusion; the education of physicians to balance the risk and benefits of blood transfusion; the avoidance of high-risk groups in campaigns for blood donations; and the evaluation of surrogate laboratory tests. That joint statement had been unanimously endorsed by the local medical directors of the Canadian Red Cross Society and adopted as working policy for the Red Cross in February 1983.

Autologous transfusion

Autologous transfusion uses the patient's own blood in treatment. When a patient is scheduled to have surgery, he or she can, time and health permitting, have a number of units of blood withdrawn on successive weeks and have that blood deposited and stored for use during the surgery. Autologous blood was, and is, regarded as the safest form of blood available for use in treatment.

In a memorandum to the medical directors dated 10 February 1983, Dr Davey said that autologous transfusion would "not be emphasized, because of logistic problems noted by some centres." Presumably, the logistic problems were that it would be difficult to institute the separate collection, storage, and inventory procedures required for autologous deposits. For the next three and a half years, the Red Cross did not provide autologous transfusion services or promote autologous transfusion except, in very exceptional circumstances, for persons with rare blood types. A committee of medical directors studied autologous transfusion in 1985, and pilot programs were developed by the Red Cross in 1987. After the success of the pilot projects, the Red Cross sought approval from the Canadian Blood Committee, the body through which the provinces funded the blood program, for the creation of a national autologous blood program. The Canadian Blood Committee refused to authorize expansion of the program, and, in fact, directed the Red Cross to phase out the pilot projects. The committee was concerned that the autologous program sent a "mixed message" to the public about the safety of the blood

supply. On 8 December 1987, after receiving advice from its advisory subcommittee, the committee authorized the implementation of an autologous program. The Red Cross was told, however, that it could not spend any additional money on the autologous program and was forbidden from promoting it.

Education of physicians

In his memorandum of 10 February 1983 about the U.S. joint statement, Dr Davey wrote to the medical directors of the seventeen Red Cross blood centres that he welcomed any initiatives by the centres to educate physicians in their areas. No evidence was presented, however, of any specific initiatives that were taken as a follow-up to his memorandum to educate physicians about the appropriate use of blood and blood products. The American Red Cross, in January 1983, provided a sample letter to its blood centres that could be sent to physicians to inform them of the relative risks and benefits of blood transfusion. In contrast, the national office of the Canadian Red Cross gave nothing to its centres to assist them in this task.

Physicians might also have been warned about the specific risk of AIDS in blood components by including a warning on the labels placed on blood components. This possibility was raised by Dr Derek Naylor, the director of blood products services of the Red Cross, in December 1984, but it went no further.

Avoidance of high-risk groups in donor recruitment

The U.S. joint statement also recommended that the persons responsible for donor recruitment should not aim their efforts at groups that had a high incidence of AIDS. In his memorandum of 10 February 1983, Dr Davey said that the recommendation should be made known to blood donor recruitment "staff." The joint statement was given to the national coordinator of the blood donor recruitment program. No further efforts in this direction were made by the national office of the blood transfusion service.

On at least one occasion, a member of the blood transfusion service advised her colleagues in blood donor recruitment to avoid targeting high-risk groups. Dr Herst, the deputy medical director of the Toronto blood centre, did so during a seminar she gave about AIDS to blood donor recruitment employees in early 1983. On that occasion, she advised blood donor recruitment employees to "not knowingly organize clinic[s] sponsored by homosexual groups or in areas that would attract gay donors." She did not know, however, whether blood donor recruitment officials changed any of the locations of clinics in response to her advice.

There is no evidence that blood donor recruitment officials, either at the national or the local level, took any steps to consider the recommendation in the joint statement. For example, clinics in Montreal continued to be held in areas of the city with large gay populations, including – between 1970

and 1987 – in the Berri-de-Montigny metro station, in the heart of the Montreal gay community. After a study in 1987 determined that there was a much higher than normal rate of infected donors at that clinic, clinics ceased to be held there.

Throughout the 1980s, blood donor recruitment services continued to use donor challenges as a means of encouraging donations. A manual for blood donor recruitment volunteers and employees, completed in August 1986, identified as key areas for recruitment the corporate and business sector, educational institutions, and community groups and associations. The manual was given to blood donor recruitment employees and volunteers. It included a covering letter from the secretary general and the president of the Red Cross that emphasized donor challenges:

Already we are seeing evidence of some very imaginative marketing approaches. In Toronto the major accounting firms have challenged each other to see who can turn out the most donors on a given day. One firm achieved 36% participation! Now the investment dealers are doing the same thing. This is only one of many new approaches we must develop to build up and maintain our donor base.

Evaluation of surrogate tests

In their joint statement of 13 January 1983, the associations representing the voluntary sector of the U.S. blood industry had said that surrogate tests were being evaluated. In its press release of 10 March 1983, the Canadian Red Cross said it would evaluate “suitable laboratory tests for AIDS that may become available, with the intention of implementing them as screening measures as soon as possible.” The reference was to the evaluation of surrogate tests. Despite these statements, the Red Cross undertook no evaluation of surrogate tests as a means to prevent HIV transmission.

Commentary

In late 1982 and early 1983, after more than a year of exponential growth in the AIDS epidemic, evidence indicated that the causative agent of AIDS was present in the U.S. blood supply. By this time, AIDS was also occurring in Canada, but no cases had, as yet, been attributed to the Canadian blood supply. The rate of reported AIDS in Canada was the highest of any country except the United States and Haiti. Senior scientists in Canada estimated that the progress of the epidemic in Canada was one and a half years behind that in the United States. Canadians thus had a vital opportunity to take preventive measures against the transmission of AIDS, including transmission through blood transfusion.

AIDS was not the first disease transmissible in blood. For years, blood transfusion services had been testing blood donations for syphilis and hepatitis B. Other pathogens, for which there was no test, were guarded against by

screening out donors who were in poor health, who had engaged in conduct that put them at risk of acquiring infectious disease, or who had been exposed to higher rates of infectious disease in other parts of the world.

It was not until the autumn of 1985 that the risk of transfusion-associated AIDS was greatly reduced in Canada. At that time, the Red Cross implemented tests for the presence of HIV antibody in all the blood donations it collected. Before testing was introduced, a variety of measures were available to reduce the risk of transmission through the blood supply.

Although other institutions were involved in the blood system, the Red Cross had the primary responsibility for implementing measures to reduce the risk of transfusion-associated AIDS in Canada, just as it had developed measures for other diseases transmissible by blood. Unfortunately, the measures taken by the Red Cross in response to the risk of transfusion-associated AIDS between 1983 and the summer of 1985 were ineffective and half-hearted. Its actions were characterized by a refusal to accept and act upon risks to which prudent blood services, elsewhere in the world, were responding. Canada thus lost the opportunity given by the one and a half years by which the epidemic in this country trailed that in the United States.

U.S. and Canadian blood bankers responded differently to the threat of AIDS. There were, of course, differences between the blood systems in the two countries and in the situation they faced in the early 1980s. The United States had the largest reported incidence of AIDS in the world, with more than four times as many cases per capita as had Canada, the country with the third-highest reported incidence. Moreover, blood shortages did not pose as large a problem in the United States as they did in Canada. A shortage in the United States could be relieved by the purchase of blood components from regions that had a surplus, either elsewhere in the United States or in Europe. In Canada, by contrast, there was little transfer of blood components among the provinces and no purchase of blood components from outside the country. Every province was responsible for the cost of collecting blood within its own boundaries. There was therefore no incentive for any province to collect more than it needed.

Perhaps the most important difference was in the role of government in supervising the blood system. U.S. public health agencies, including the Centers for Disease Control, showed leadership by engaging in discussion with the blood industry about methods of reducing the risk of AIDS in blood. The U.S. Food and Drug Administration exercised a regulatory function over the U.S. blood industry. It licensed and inspected blood banks that were involved in interstate commerce. It not only made regulations, but also supervised the blood industry by issuing guidelines and recommendations that were more than advisory. Compliance by the blood industry was expected and obtained. In Canada, the federal government regulated the manufacture of blood products and the collection of plasma by plasmapheresis, but it did not actively regulate the collection and processing of whole blood. Unlike

its U.S. counterpart, the Department of National Health and Welfare never issued guidelines or recommendations for the collection of blood in Canada. Until the summer of 1985, neither the federal government nor the provincial governments gave the Red Cross directions or showed any leadership in helping the Red Cross to cope with issues of transfusion-associated AIDS.

Despite the differences between the two countries, there were many similarities. There was also a common border and easy travel between the two countries. Many gay men in Canada travelled to cities in the United States where the incidence of AIDS was high. Cultural and social similarities between the two countries made it reasonable to expect that AIDS would spread in Canada in the same way that it had in the United States. The blood collector in Canada was part of the same international organization as the largest voluntary blood collector in the United States. The American Red Cross and the Canadian Red Cross used similar recruiting measures and shared information frequently, by correspondence and by attendance at each other's meetings. It can fairly be said that the national office of the Canadian Red Cross was as well informed about the U.S. blood system as were most U.S. blood bankers. Although the Canadian Red Cross did not have the benefit of assistance and direction from governments in Canada with respect to measures to reduce the risk of transfusion-associated AIDS, it was aware of the guidelines and recommendations issued by the U.S. governmental authorities for blood banks in that country.

Because of these similarities and because of the fact that Canada possessed one of the highest reported rates of AIDS in the world, one would have expected the Canadian Red Cross to follow the measures for risk reduction that had been adopted in the United States or to develop equally effective measures of its own for reducing the risk.

Measures taken in the United States to reduce the risk of contamination

In December 1982 and January 1983, U.S. blood bankers, encouraged by public health authorities, began to take measures to prevent persons at high risk of contracting AIDS from donating. The vast majority of persons infected with AIDS had been classified by U.S. public health agencies as falling into specific groups. Seventy-five per cent of them were homosexual or bisexual men. Twelve to 15 per cent were intravenous drug users. Blood bankers sought ways to discourage, prevent, or restrict persons within these groups from donating blood and to ensure, to the best of their means, that any blood that was donated by members of these high-risk groups would not be used for transfusion.

In early 1983, the blood bankers had considered five main types of measures to achieve these goals. Each type constituted a different layer of safety. The first was an educational campaign, designed to inform the general public about the groups that were at high risk of contracting AIDS and to ask members of those groups not to go to blood clinics, donate blood, or sell plasma. At that time the high-risk groups were described as: homosexual

or bisexual men with multiple partners, recent immigrants from Haiti, persons possessing the signs or symptoms of AIDS, intravenous drug abusers, and sexual partners of persons at risk of contracting AIDS. The second type of measure was to give information to persons who attended the clinics. This information described the groups at high risk of contracting AIDS and the signs and symptoms of AIDS, and asked persons who were at high risk or who had signs or symptoms of AIDS not to donate. The third type of measure was to question potential donors orally, or by a written questionnaire, to discover whether they belonged to a high-risk group or had any of the signs or symptoms of AIDS, and to prevent anyone who answered positively from donating. The fourth type of measure was to examine potential donors physically to determine whether they possessed any signs or symptoms of AIDS or its precursor states, and to prevent anyone with such signs or symptoms from donating. The fifth type of measure was to conduct surrogate tests on blood donations and to discard the donations that reacted positively.

At a meeting in January 1983, blood bankers from the voluntary sector of the U.S. blood industry, represented by the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers, decided to implement only one of the five types of measures. They announced in a joint statement, dated 13 January 1983, that they would carry out direct questioning of donors about signs and symptoms of AIDS and its precursor states. The questioning of donors about their membership in a high-risk group or involvement in a high-risk activity was rejected. The blood bankers feared that donors would be offended and that there would be a reaction from militant gay organizations. Surrogate tests were rejected because of uncertainty about their efficacy, an increased cost of approximately \$5.00 per unit, and a loss of approximately 3 per cent of donations that could be expected to test positive.

Early in March 1983, the U.S. Department of Health and Human Services recommended that persons at high risk of contracting AIDS refrain from donating blood and that all potential donors be informed of that recommendation. Within days, pamphlets describing the high-risk groups and signs and symptoms of AIDS were in place at volunteer blood banks in the United States. Measures were taken to ensure that donors read the pamphlet, either by acknowledging on a copy of it that they had done so or by answering a question during an interview by a nurse. In the next few months similar pamphlets were distributed by blood transfusion services in Europe, Australia, and other countries where the rate of AIDS was also increasing but still was less than that in Canada. Over the next year, U.S. blood collectors refined their pamphlets, using more precise descriptions of the high-risk groups. By the spring of 1983, in short, they had implemented the first two measures of risk reduction and a part of the third measure, but had not implemented the other two.

A committee of the U.S. Institute of Medicine recently studied and reported on the response of the U.S. blood system to the AIDS epidemic in the 1980s. It approved of the donor-deferral measures that were adopted by the blood bankers, but concluded that donors should have been directly questioned as early as January 1983 about membership in groups at high risk of contracting AIDS.

Measures taken to discourage high-risk donors in Canada

The risk-reduction measures used in Canada can be summarized briefly. As early as January 1983, the Canadian Red Cross Society proposed that it would adopt the joint statement of the U.S. blood bankers as a working policy, subject to approval by the medical directors of its seventeen blood centres. That approval was given unanimously. In the months that followed, the Red Cross did not, however, implement any of the recommendations in the joint statement. In particular it did not implement the recommendation that "all donors should be asked questions designed to elicit a history of night sweats, unexplained fevers, unexpected weight loss, lymphadenopathy or Kaposi's sarcoma," the signs and symptoms of AIDS. In February, the Canadian Hemophilia Society was left with the understanding that the Red Cross would add questions about the symptoms of AIDS to its questionnaire for donors. In March, the Red Cross issued a press release that listed several steps it would take to protect blood recipients from the possible transmission of AIDS through blood. The first of these was to ask "specific questions to detect potential donors with symptoms of AIDS or who might be carriers of AIDS." Despite this public undertaking and the recommendation of its local medical directors that these questions be asked, the Red Cross merely amended its donor questionnaire to include, in its preamble, that it was important that donors be "in good health." Moreover, the assistant national director of the blood transfusion service, Dr Martin Davey, instructed local medical directors not to question donors about symptoms.

Voluntary self-exclusion

The principal method developed by the national office of the Red Cross to prevent persons at high risk of contracting AIDS from donating was "voluntary self-exclusion." This was different from "active deferral" by which, for example, donors are asked whether they belong to high-risk groups or engage in high-risk behaviour and, if they answer affirmatively, are excluded from donating. Voluntary self-exclusion was a passive measure under which the Red Cross would never have to tell any donors that they could not donate blood because they were at high risk of contracting and transmitting AIDS. It was left to the donors to decide whether they wished to give blood. The fundamental premise of voluntary self-exclusion was that volunteer donors who gave blood for altruistic reasons would, if informed that they presented a risk to the blood supply, refrain from donating blood. The success of this

policy was therefore entirely dependent on communicating successfully to all potential donors, either before they came to the clinic or at the clinic, that persons at high risk of contracting AIDS ought not to donate blood.

The Red Cross employed two means of carrying out voluntary self-exclusion. The first was a series of public statements describing the groups at risk of contracting AIDS and asking members of those groups not to donate blood. The second was to communicate with representatives of high-risk groups, particularly in gay organizations, and through them to disseminate the message that persons at high risk ought not to donate.

The Red Cross was a large and sophisticated organization. It had extensive experience in public relations and public communication and devoted much of its energy to these tasks. It is surprising that it engaged in little planning of and research into effective means of communicating the message of self-exclusion. Before launching its public information campaign, the Red Cross did not consult public health officials or organizations representing high-risk groups about the best ways to reach persons at high risk of contracting AIDS. It conducted no research into the best way of communicating the message. Its public information campaign consisted primarily of two press releases issued by its national office, one in March and one in July 1983.

The press releases received relatively little attention, as was confirmed, in September 1983, by a Red Cross analysis of its newspaper clippings. It was clear in any case that two press releases alone could not possibly reach all the persons the Red Cross hoped to inform. Estimates of the number of homosexual and bisexual men in Canada range from 2 to 10 per cent of the male population. It should have been obvious that repeated messages communicated through a variety of media were necessary to reach so large and diverse a group effectively. Although there was some additional communication with local media by some local medical directors, there was no concerted effort of repeated messages intended for this group.

The other method adopted to encourage voluntary self-exclusion was direct communication by the Red Cross with representatives of high-risk groups. In practice, this meant communicating with representatives of the gay community. This was to have been done both at the national level by the national office of the blood transfusion service and at the local level by the medical directors of the seventeen blood centres. It was obvious that there was no single organization that represented or could communicate with all men who had sex with men. The only nationally distributed Canadian publication for a gay audience was *The Body Politic*. Its distribution was limited and could reach only a small proportion of all gay persons, and only those who understood English. As a first step in communicating the message of self-exclusion, local medical directors needed to meet with members of their local gay community organizations. They were not instructed to do this until July 1983, with little or no assistance or supervision provided by the national

office. Predictably, the responses of the medical directors varied, depending upon their initiative, their imagination, and probably their attitude towards homosexuality. Some made significant efforts. Some made no effort.

It was unrealistic to believe that this method – communicating with representatives of the gay community – would reach all, or even most, men at high risk of contracting AIDS. First, only some men at high risk read gay newspapers and took part in gay community activities. Many men who had sex with men did not identify themselves, either publicly or privately, as gay. In addition, gay community organizations had few of the resources they would need to tell gay persons that they should not donate blood.

It was inevitable then that persons at high risk would appear at blood clinics to donate blood. It was obvious to local medical directors and the national office, certainly by the summer of 1983, that a second level of safety was needed. Potential donors should have been told, when they came to the clinic, about the groups that were at high risk of contracting AIDS and about the signs and symptoms of AIDS.

Community-based measures to prevent contamination

It is difficult to determine precisely the effect that community organizations and physicians serving gay communities had in discouraging persons at high risk of contracting AIDS from donating blood. There is, however, some evidence from British Columbia, where the community efforts were earliest and most intense, that they did reduce the incidence of transfusion-associated HIV infection.

Dr Robert S. Remis, an epidemiologist, formerly the director of the regional bureau of infectious diseases in Montreal and now a consulting epidemiologist with the AIDS bureau of the Ontario Ministry of Health and an associate professor in the department of health sciences of the Faculty of Medicine at the University of Toronto, has calculated the number of cases of transfusion-associated HIV infection by region for each year between 1978 and 1985. In most regions in Canada the number of cases grew each year, yet in British Columbia the number of cases of transfusion-associated HIV declined after 1982. Dr Remis also calculated the number of transfusion-associated AIDS cases that might be expected in each province based on the prevalence of AIDS in that province, and compared that number with the actual number of cases in each province. Because of the large gay population in Vancouver, it was expected that the incidence of AIDS in British Columbia, and consequently the rate of transfusion-associated AIDS, would be one of the highest in Canada. British Columbia had the highest prevalence of AIDS of any province, but Dr Remis found that it had one of the lowest rates of transfusion-associated AIDS in the country – less than half the number that was expected.

The efforts of the Red Cross to promote the message of voluntary self-exclusion were no more extensive in British Columbia than elsewhere. Indeed, the medical directors of the blood centres in St John's, Saskatoon, and Winnipeg were much more active in their communications with the gay community than were the medical directors of the Vancouver blood centre. What was different in Vancouver, however, was the manner in which the message not to donate blood was delivered and the content of the message. The message was delivered consistently and frequently, at information forums, at monthly meetings, in posters, and by physicians to their gay patients. AIDS Vancouver and physicians serving the gay community were highly organized and hard working. It can be inferred that similar activities undertaken in other parts of Canada, although not as extensive as those in Vancouver, undoubtedly had a positive effect in discouraging persons at high risk of contracting AIDS from donating blood.

In their efforts to support the policy of self-exclusion, the community organizations had little meaningful assistance from the Red Cross. An exception was in Winnipeg, where Dr Schroeder approved the pamphlet produced by the Manitoba Gay Coalition and took part in an information forum in August 1983.

The Red Cross had much to learn from community organizations in its efforts to promote a policy of voluntary self-exclusion. It could have learned whether its educational materials were effective in communicating to gay persons at high risk of contracting AIDS. It could have learned whether its definition of high-risk groups was easily understood. The pamphlet issued by the Manitoba Gay Coalition in August 1983, for example, explained much more clearly which gay men should not donate blood than did the Red Cross pamphlets of 1984 and 1985. The same pamphlet suggested that gay men who had donated blood could telephone the Red Cross afterwards and say that their donation should be used "for research purposes only." The Red Cross did not make a similar suggestion in its pamphlet until November 1986.

Development of a pamphlet by the Red Cross

The Red Cross did not begin to create a pamphlet that described the groups at high risk of contracting AIDS until July 1983, four months after pamphlets of this nature were being distributed in the United States. It took the Red Cross an additional ten months, until May 1984, to produce a pamphlet about AIDS that was little more than 400 words long, and to start using the pamphlet in its blood clinics as a means of discouraging high-risk donors. Until pamphlets were distributed, the existing questionnaire about the donor's health was the only measure used at most blood clinics to defer high-risk donors. It did not mention AIDS, the symptoms of AIDS, or the persons most at risk of contracting AIDS. It merely had a preamble that said donors should be in good health. Nor was there anything at most blood donor clinics to alert persons

at risk of contracting AIDS that they should not donate blood. Those who had not heard about voluntary self-exclusion (and there inevitably would be many) were thus not discouraged from donating blood.

There is no reasonable explanation for the length of time it took the Canadian Red Cross to prepare the pamphlet about AIDS, particularly when it is compared to the time it took other blood services throughout the world to prepare pamphlets or information sheets for donors. Blood collectors in the United States put pamphlets in place within days of being told to do so by the Department of Health and Human Services. European countries that had not already done so followed suit in the spring and early summer of 1983, soon after similar recommendations were made by the Council of Europe.

The Red Cross's development of a pamphlet was slow and bureaucratic. The pamphlet was discussed and studied by a series of committees and subjected to a series of approvals. Part of the reason for this convoluted process was undoubtedly the separation between the blood transfusion service and the blood donor recruitment program. According to the division of responsibilities in the Red Cross, blood donors were the "property" of the blood donor recruitment program. The blood transfusion service did not have the authority, or the budget, to prepare and distribute a pamphlet to donors without the collaboration of the blood donor recruitment program. For its part, the staff of the blood donor recruitment program had little involvement in or understanding of the issues raised by AIDS. Volunteers in the blood donor recruitment program were ill-suited to deliver a message concerning homosexuality that would result in the exclusion of donors. This was apparent when in early July 1983, during a period of chronic shortages, a representative of the blood donor recruitment program was interviewed on radio in Toronto about an appeal for blood donors. Asked directly who should not give blood, the representative made no mention of persons at risk of contracting AIDS.

The pamphlet that was finally distributed in the spring of 1984 for use at blood donation clinics, moreover, contained an outmoded description of persons at high risk of contracting AIDS. It referred to "homosexual or bisexual men with multiple partners." This language was vague and confusing. Earlier in the year, the American Red Cross had defined "multiple partners" in a revised pamphlet as "more than one." The Canadian Red Cross pamphlet did not describe the symptoms of AIDS or its precursor states. Unlike the pamphlet used by the American Red Cross at the time, it included no statement that donors at high risk of contracting AIDS who had donated blood could telephone the blood centre afterwards and ask that the donation not be used for transfusion. Such a notice would have been valuable, because it was inevitable that some persons at high risk, whose sexual preferences were unknown to their co-workers, would find themselves at Red Cross clinics with their colleagues as part of a donor challenge. Given the lack of privacy in clinics, there was no means by which such "closeted" donors could exclude

themselves without possible public embarrassment. The Canadian Red Cross did not adopt an alternative approach, the confidential unit exclusion program used by the New York Blood Center, until much later.

Pamphlets were a potentially important method of informing high-risk donors that they should not donate. To be effective, however, a pamphlet had to be comprehensible and unambiguous; it had to be made available to all donors; and all donors had to be required to read it. The Red Cross pamphlet, and the way in which it was used, met none of these requirements.

The message was not readily comprehensible. Its language required a higher level of literacy than many donors possessed. The definition of gay men at high risk of contracting AIDS was vague and confusing. Even though many months were spent developing the pamphlet, none of the time or energy went into research, by such means as focus groups, about the kind of language that would best communicate the message to all donors.

The pamphlet was published in English- and French-language versions, but some blood centres that needed copies in both languages were not sent enough copies. There were no pamphlets in other languages, despite the fact that there were significant numbers of persons, particularly in the cities with the highest incidence of AIDS, who did not speak English or French fluently. A three-month supply of pamphlets was produced for what was supposed to be a three-month pilot project.

Some donors were not given the pamphlet, while others were not required to read it by the Red Cross employees or volunteers at the clinic. There was no way to be certain that donors read the pamphlet, since they were not required to acknowledge that they had done so. The AIDS information pamphlet was treated differently from the Red Cross health questionnaire, which was administered as part of the donation procedure and in the same manner at clinics throughout Canada. In contrast, there was little uniformity in the way that the AIDS pamphlet was given to donors to read. Some blood centres, following the instructions of the national office, handed out copies as part of the pre-donation procedure. Some centres handed them out during the donation or afterwards. Since there was no way provided for a person to withdraw his or her donation, handing out the pamphlet during or after the donation was useless.

After six months, the national office had not said whether the pilot project should continue. In late December 1984 and early January 1985, a survey of the blood centres revealed that, after eight months, many still had significant quantities of their original three-month supply of pamphlets. Other centres had exhausted their supply. Even if some pamphlets were being reused, it is clear, as the Red Cross director of nursing concluded in January 1985, that the pamphlets were not being used universally. This troubled some members of the Red Cross board of directors, who voiced concern about potential liability for cases of transfusion-associated AIDS.

The Red Cross distributed a new pamphlet in August 1985, only a few months before testing began for HIV antibody in all blood donated in Canada. That pamphlet included in its list of high-risk groups "active homosexual or bisexual males." Even after the introduction of testing, pamphlets continued to be important in preventing the transmission of AIDS because of the "window period," during which HIV infection would not be detected by the test. It was not until January 1986 that the pamphlet was revised to define unequivocally the largest group at high risk of contracting AIDS as "any male who has had sex with another male since 1977." It was only in November 1986 that the pamphlet was further revised to announce that a donation could be withdrawn after it was given. This was a year after HIV-antibody testing had been introduced for all blood donations in Canada and almost three years after a similar provision for withdrawal had been added to U.S. pamphlets.

It has been suggested by the Red Cross that local medical directors always had the discretion to refuse to accept a donation from someone who appeared not to be healthy, and that in this way they could screen out persons at high risk of contracting AIDS. Several medical directors testified that they or their staff tagged donations from donors suspected of being at high risk and then destroyed the donations later. In practice this meant that someone at a blood clinic, usually a nurse, decided by looking at someone that he was gay. This practice assumed that gay persons were identifiable and was premised on stereotypes. It was unscientific and was no substitute for any of the safety measures contemplated at that time, including the least intrusive – giving persons at risk the information that would allow them to recognize that they should not donate and a means of withdrawing themselves or their donation without embarrassment. Moreover, it was wrong to mislead donors into believing that their donations would be used.

Competing concerns

The Red Cross was not publicly forthcoming about the extent of its risk-reduction measures. In its 10 March 1983 press release, the Red Cross announced that it would question donors about the symptoms of AIDS. It soon changed its policy and not only did nothing to correct the misimpression that had been created, but actually encouraged it. The Red Cross sought the endorsement of the National Advisory Committee on AIDS for the measures promised in its press release without informing the advisory committee that it had since changed its policy regarding questioning donors about signs and symptoms of AIDS.

The Red Cross wanted to answer the concern of the public that something be done to protect the blood supply from AIDS without having to take measures that would result in rejecting donors or that might give offence. It

avoided all controversy. An example of its caution occurred in July 1983. At that time one of its employees said at a press conference that the Red Cross was discouraging homosexuals from donating blood. This was the appropriate policy to have at the time, given what was known about the disease, and it was consistent with the recognition, reflected in pamphlets distributed in blood centres in the United States, that there was a risk of AIDS from a single homosexual contact. As soon as the Red Cross announced this policy, which had not been previously communicated to representatives of the gay community, it was met with controversy. Rather than facing the controversy and continuing with a policy that it knew to be sound, the Red Cross renounced the policy and returned to its earlier, less precise definition.

It is understandable that the Red Cross should not want to offend donors. Discrimination against groups such as Haitians or homosexual men was anathema to the Red Cross and, in its eyes, inconsistent with its identity as a humanitarian organization and contrary to its founding principles. At the same time, it was essential for the safety of the blood supply that effective measures for risk reduction be implemented, even if they created controversy.

It was also understandable that the Red Cross should be concerned about shortages of donated blood. Throughout the early 1980s there had been increasingly severe shortages of blood components in Montreal, Toronto, and Vancouver, which together used 65 per cent of the blood supply in Canada. The Red Cross had no control over the demand for its blood components. Any reduction in supply caused by a loss of donors would therefore aggravate existing shortages.

Had the Canadian blood system not discouraged interprovincial transfers of blood, the shortages could have been met, in part or totally, by transfers from those regions capable of producing more than their need to those regions that could not produce what they required. One would think that the sharing of resources in this manner would have been a principal benefit of a national blood system. That was not the case in Canada.

One would also have expected that the Red Cross would carefully weigh its concerns about shortages of blood components and about potential discrimination against high-risk groups against the possibility that AIDS, a fatal disease, could infect the blood supply. Given the then current knowledge of AIDS, the strategies which the Red Cross said publicly in March 1983 it would undertake – that is, the direct questioning of donors about signs and symptoms of AIDS in addition to voluntary self-exclusion – would not, if assiduously carried out, have tipped the scales unreasonably. Concerns about discrimination could have been met by providing some means, either by a subsequent telephone call or by a written confidential unit exclusion, that would allow men who had had sex with men to withdraw their donation without public disclosure of their sexual preference.

Assessment of risk

The Red Cross did not carry out risk-reduction measures assiduously. It did not appropriately weigh the competing concerns. Rather, it consistently used the absence of "definitive proof" of a link between AIDS and blood transfusion as a justification for maintaining the status quo. Its employees or officials repeatedly expressed the view that the threat from AIDS to the blood supply was not sufficient to require a significant change in its donor-screening measures.

One such assertion was made in December 1982, when Dr Martin Davey and Dr John Derrick, the director of blood products services, wrote to the medical directors of the Red Cross blood centres that the evidence of transmission of AIDS through blood was not clear enough to warrant excluding persons at high risk from donating blood. Dr Derrick was quoted as reiterating this position in a March 1983 article in *The Body Politic*. Even after the press release issued in March 1983 announcing the policy of voluntary self-exclusion, senior officials of the Red Cross considered the risk of AIDS to be remote. Dr Davey wrote at the end of May 1983 that the risk of AIDS was very low and that it "may not even be significant." In a briefing paper written in October 1983, Dr Derrick expressed the view that screening measures taken in the United States were in response to "pressures exerted by the media, user groups and other special interest groups." In December 1983, Dr Derrick wrote to local medical directors that, even though the agent that caused AIDS was "probably blood borne," the danger of "AIDS developing as an outcome of transfusion of blood or blood components would appear to be minuscule" and that there were "many now who consider that the importance of AIDS as a threat to public health in this country has been overrated." By January 1984 (when the *New England Journal of Medicine* published a report, by Dr James Curran and colleagues at the Centers for Disease Control in Atlanta, of eighteen cases of transfusion-associated AIDS in the United States), the link between AIDS and blood transfusion was established to the satisfaction of even the most sceptical of U.S. blood collectors. To the Canadian Red Cross, the report was merely another piece of evidence that, according to Dr Davey, "increased the odds" that AIDS could be transmitted through blood.

The Red Cross should not have required conclusive evidence before taking strong action to reduce the risk of AIDS. It was given sound advice by its honorary counsel, Michael Worsoff, as early as 29 March 1983:

The evidence of possible unacceptability of the blood does not have to be conclusive – the decision can be made on a basis of "reasonable doubt" as to its suitability. With reference to the AIDS problem in particular, the premise is not that Canadian Red Cross has to justify beyond any scientific doubt that there is a link between the designated "high risk groups" and the development of AIDS since, if there is even a possibility of transmission via blood, CRC [Canadian Red Cross] has the moral and legal obligation to protect the blood recipient above all.

The Red Cross would have done well to heed this advice. Where there is reasonable evidence of an impending threat to public health, it is inappropriate to require proof of causation beyond a reasonable doubt before taking steps to avert the threat. As an editorial in the *American Journal of Public Health* in May 1984 put it:

The incomplete state of our knowledge must not serve as an excuse for failure to take prudent action. Public health has never clung to the principle that complete knowledge about a potential health hazard is a prerequisite for action. Quite the contrary, the historical record shows that public health's finest hours often occurred when vigorous preventive action preceded the crossing of every scientific "t" and the dotting of every epidemiological "i".

Perhaps the best indication of the Red Cross's lack of appreciation of the risk of transmitting AIDS through blood was expressed in July 1985, when Dr Davey said that if HIV-antibody testing had been carried out for the previous five years, only three cases of transfusion-associated AIDS would have been prevented. He was wrong.

In evaluating the actions of the past, one must always be mindful of the danger of doing so with the benefit of hindsight. It would be unfair to criticize the conduct and decisions of persons and institutions about AIDS in the 1980s from the perspective of our knowledge in the 1990s. I have assessed the measures taken by the Red Cross to reduce the risk of transmission of AIDS through the blood supply not on the basis of today's knowledge but, rather, on the basis of the knowledge at that time that AIDS represented a significant, although unproven, risk to the blood supply. The information known in the period examined in this chapter was sufficient for public health officials, regulators, and blood bankers in the United States, western Europe, and Australia to take preventive action to restrict the blood supply from persons at high risk of contracting AIDS. It should have prompted a similar response in Canada.

The Red Cross has made the following submission:

While in 1983 and 1984, CRCS [Canadian Red Cross Society] donor screening measures differed from some of those in other countries, in particular the United States, the data demonstrates that the CRCS did as well, or even better, than most other countries, as measured by incidence of TAA [transfusion-associated AIDS] and AIDS associated with component therapy.

The incidence of transfusion-associated AIDS in Canada reflects the actions, and the inactions, of all persons and institutions that had any impact upon it. It is influenced by the effects of individual decisions, such as those of a

physician who chose not to use blood during surgery and a person who chose not to donate. It is also influenced by the efforts or failures of public health departments and gay community organizations to communicate the message that persons at risk of contracting AIDS should not donate blood. The rate of transfusion-associated AIDS is not the result of the effects of measures implemented by any one person or organization. It is impossible to draw any conclusion about the performance of the Red Cross from a comparison of the incidence of transfusion-associated AIDS in Canada with the incidence of transfusion-associated AIDS in other countries. The question should not be how well Canada did compared with other countries. The question is, in the light of what was known at the time about the risk of transfusion-associated AIDS and the measures that were available to reduce that risk, was enough done? The answer is no. If the Red Cross had taken more vigorous measures to reduce the risk of transmission, the incidence of transfusion-associated AIDS would have been reduced and Canada's standing, compared to that of other countries, would have been higher.

12

The Introduction of Testing for HIV Antibody

One of the most effective means of protecting the safety of the blood supply is to test blood donations for disease-causing organisms that may be present. Before the emergence of the human immunodeficiency virus, or HIV, in the blood supply, the Canadian Red Cross Society (Red Cross) already had considerable experience in testing. It had been testing all blood donations for the presence of syphilis since 1949 and hepatitis B since the early 1970s.

Soon after the discovery in April 1984 of the virus that causes AIDS (eventually named HIV), a test was developed that could identify whether a person had been exposed to infection by identifying the presence of antibodies to that virus. This test was initially available only in research laboratories where individual tests were made by hand. In the summer of 1984, however, work began in the United States on developing commercial kits that could test for the presence of the HIV antibody and could be made widely available for testing blood donations.

By August 1984, the Red Cross recognized that such kits would be available within a year and that testing for HIV antibody should be implemented without delay. Test kits were licensed in the United States at the beginning of March 1985, and wide-scale testing of blood donations for HIV antibody began there within a few weeks. In Australia, testing began in mid-April 1985 and was fully implemented the next month. By contrast, in Canada, an implementation plan for testing blood donations for HIV antibody was not prepared by the Red Cross until 1 May 1985, and funding for it was not authorized by the Canadian Blood Committee for another three months. Testing was not in place throughout Canada until the beginning of November 1985.

The delay in HIV testing in Canada was a matter of concern well before the creation of this Inquiry. In particular, the subcommittee on Health Issues of the House of Commons Standing Committee on Health and Welfare, Social Affairs, Seniors and the Status of Women had investigated the contamination of blood and blood products with HIV in the 1980s and had

concluded, even after hearing considerable evidence, that many questions remained unanswered. Those questions in no small part gave rise to the committee's recommendation that this Inquiry be held. The committee said:

With respect to the introduction of the ELISA [enzyme-linked immuno-sorbent assay] test for blood screening, the period from May 1984, when a description of a laboratory assay for HIV antibodies was published in a major scientific journal, to May 1985, when the Red Cross submitted its implementation plan to the Canadian Blood Committee, must be closely examined. A question of major importance concerns the development of the Red Cross implementation plan for blood screening. Was it not possible to have developed the plan in a shorter period of time, so that the key decisions on implementation could also have been made earlier?

The events from May 1 to August 1, 1985 must also be clarified fully. The three-month period that the Canadian Blood Committee took to approve funding for the Red Cross implementation plan must be explained. Given the fact that the blood system was confronted with a major crisis, was it not possible for contingency funding to have been made available prior to May 1, so that implementation of the testing plan could have proceeded more quickly?

All of the available documentation, whether in the form of correspondence between the various players in the system, or minutes of meetings, must be made public and carefully reviewed. Of particular interest is the Consensus Meeting of provincial and territorial representatives of 4 July 1985. Almost four weeks elapsed after that meeting before the Red Cross plan was finally approved: the delay in Ontario's decision alone accounted for half of that four-week period.

The Red Cross suggestion that there might have been a shortage of commercial test kits on the international market until the fall of 1985 must be fully assessed. The available correspondence and inventory records of the Canadian Red Cross and the various companies involved, and the minutes of meetings of the Canadian Blood Committee must be made public, to the fullest extent possible.

Throughout the course of this Inquiry's hearings, other questions emerged. What role should the federal government have played in the introduction of testing? To what extent did the difficulties in the relationship between the Red Cross and the Canadian Blood Committee impede the introduction of testing? Did other factors, such as the need for alternative test sites, complicate and slow the introduction of testing?

This chapter examines the implementation of HIV-antibody testing from the time of the identification of the virus, which brought with it the technical possibility of testing for it, to the time when HIV testing was implemented in every blood centre in Canada. Finally, the causes of delay are analysed.

April 1984: Identification of the virus

In May 1983, Dr Luc Montagnier of the Pasteur Institute in Paris had isolated a virus, which he named LAV (lymphadenopathy-associated virus), that he believed to be the causative agent of AIDS. His work, although not fully appreciated at the time, became the basis for the development of tests to detect the virus and its antibodies. In April 1984, Dr Robert Gallo of the National Institutes of Health in the United States and his team of researchers isolated the virus that was the causative agent of AIDS. He named this virus HTLV-III (human T-cell lymphotropic virus). This was the same virus that Dr Montagnier had found, and while at the time it was announced that the isolation had occurred independently of Dr Montagnier's work, it was later found that Dr Gallo's discovery was based, in part, on a sample of the virus provided by Dr Montagnier's laboratory. Dr Gallo produced a reagent capable of reacting with HTLV-III antibody present in blood serum. He was therefore able to test blood samples for the presence of HTLV-III antibody. A few weeks later a third scientist, Dr Jay A. Levy of the University of California at Berkeley, also isolated the virus, which he named ARV (AIDS-related virus). Eventually, in 1986, the virus became known as HIV (human immunodeficiency virus), and for convenience that name is used throughout this chapter.

Soon after Dr Gallo developed the test for HIV antibody, he shared his expertise and resources with the Canadian government, which developed a similar test at the Laboratory Centre for Disease Control in Ottawa in the summer of 1984. This test was performed on only a limited basis in research laboratories. It was not widely accessible.

On 23 April 1984, the U.S. Secretary of Health, Margaret Heckler, announced that within approximately six months HIV-antibody tests would be widely available and within approximately two years an AIDS vaccine would be available in the United States. Her prediction of a vaccine was overly optimistic; more than thirteen years later there is still no licensed vaccine for AIDS. Her prediction of a widely available blood test proved to be more accurate. HIV-antibody test kits were licensed and available in the United States at the beginning of March 1985, a little more than ten months after her announcement.

According to Dr Thomas Zuck, a former director of the Division of Blood and Blood Products of the U.S. Food and Drug Administration, the prediction had an unfortunate effect. It dampened interest throughout the blood-banking community in surrogate testing, which had by then been instituted in the United States by the Irwin Memorial Blood Bank in San Francisco, four other California blood centres, and a commercial plasma fractionator, also in California. Surrogate tests did not test for AIDS or its causative agent, but rather tested for markers of other infections that were prevalent among persons infected with AIDS. The most common surrogate test was for the hepatitis B core antibody. Another surrogate test used in some places, the alanine amino transferase (ALT) test, measured liver function.

In 1984, two methods were commonly used to test blood samples for HIV antibody. The first was an enzyme-linked immunosorbent assay (ELISA). No commercial kits were available. Each test had to be made by hand in the laboratory. The ELISA test was prepared by taking the reagent, which contained the antigen (the substance capable of inducing an immune response) obtained from inactivated HIV, and coating it on a plate with a number of wells. Although inactivated and non-infectious, the reagent was still able to bind HIV antibodies. The test was performed by diluting serum from a person's blood sample and adding it to one of the wells on the plate. If the person's blood contained HIV antibody, the serum would react with the HIV antigen on the plate. The reaction was made visible by adding reagents that caused a colour change.

The ELISA test had a high sensitivity but a low specificity. It was designed as a screening test and was sensitive enough to pick up the vast majority of infected samples, but it would show as positive many more samples that did not in fact contain HIV antibody. At the time, out of 100 ELISA positive reactions only ten were true positives (a specificity of 10 per cent). It was therefore a poor diagnostic test because, most of the time, it would not accurately diagnose the antibody status of the donor.

The second, or confirmatory, test for identifying HIV antibody available in 1984 was the western blot test. This is a much more complicated test, more difficult and more expensive. It is performed by separating, using an electric field, "disrupted" HIV into its various proteins, transferring the proteins to paper, and adding the sample being tested to see whether antibodies in the sample will react with any of the HIV proteins. The various proteins are illustrated on paper as a line each. The completed test resembles a bar code. The western blot test was not confirmatory in the strict sense of the word because, like the ELISA test, it tested for HIV antibody rather than the virus itself. It was, however, much more specific because it showed each of the proteins to which a particular sample reacted. Although the western blot test was widely used, the interpretation of its results did not become standardized until the latter part of the 1980s. The cost of performing a western blot test was approximately \$100. By comparison, an ELISA test cost about \$4.

Now that it was possible to identify the presence of HIV antibody, researchers debated the meaning of a positive reaction. Did the presence of HIV antibody indicate infection with, or immunity against, the virus? How many of those infected would go on to suffer symptoms of the disease? How infectious were people who were infected but did not yet show symptoms? Some experts, including Dr Gallo himself, believed that HIV was like rabies, in that a person would be on the way to developing AIDS after a single exposure. Others, including Dr Peter Gill, director of the Bureau of Microbiology at the Laboratory Centre for Disease Control in Ottawa, thought additional causes or "co-factors" played a role in the development and rate of development of AIDS. Some experts even doubted – and still doubt – whether HIV causes AIDS.

August 1984: Preparations for HIV-antibody testing

By the beginning of August 1984, despite debates over the exact significance of HIV antibody, there was ample justification to remove from the blood supply units of blood that were reactive for it. On 2 August 1984, Dr John Derrick, the Red Cross's adviser on regulatory affairs and good manufacturing practices and later head of the Red Cross AIDS project, told Dr Roger Perrault, the national director of the blood transfusion service, that evidence correlating the presence of HIV antibodies with development of AIDS was "sufficiently strong to warrant acceptance of a positive test" as an indicator of infection. A method of identifying HIV antibody thus could be used to test blood donations for the purpose of removing infected donations from the blood supply. He wrote to Dr Perrault advising him that test kits would be available from U.S. sources within a year and that pressures to institute the test would be too strong to permit delay in its implementation. Dr Derrick recommended that the Red Cross be prepared to implement the test in 1985. He further recommended that the Red Cross approach the National Advisory Committee on AIDS for help in dealing with some of the issues surrounding HIV-antibody testing. One of these issues was the possibility that persons would donate blood solely to find out whether they were HIV positive, with the result that the blood supply might be contaminated by an undetected infected donation. On 9 August 1984, he wrote asking for such assistance to Dr Alastair Clayton, the director general of the Laboratory Centre for Disease Control, which acted as the secretariat for the National Advisory Committee on AIDS.

The National Advisory Committee on AIDS was a committee appointed in 1983 by the Minister of National Health and Welfare to give advice about AIDS to the Minister and the Department of National Health and Welfare, particularly the Laboratory Centre for Disease Control. The committee also gave advice to researchers and other non-governmental organizations when appropriate. Its membership included a number of scientists working in epidemiology, immunology, and virology, together with Dr Perrault of the Red Cross, Dr Denise Leclerc-Chevalier, executive director of the Canadian Blood Committee, and Dr Clayton. The provincial public health departments were not represented. Members of the committee were appointed for their individual expertise and not as representatives of particular organizations. Dr Richard Mathias, an epidemiologist and a member of the committee, was asked at the Inquiry whether anyone on the committee was capable of critically evaluating the positions taken by the Red Cross. He said:

When we started this it was clear that members of NACAIDS [National Advisory Committee on AIDS] were there for their individual expertise. So my answer to your question would be, "Yes, indeed there was a Canadian expert there, and it was Dr Roger Perrault, who was there in his capacity as an expert to be part of the NACAIDS thing." He was not there representing the Red Cross.

Dr Perrault believed the opposite. He testified that he participated in the committee as a representative of the Red Cross.

The National Advisory Committee on AIDS reported to the Minister of National Health and Welfare through the Laboratory Centre for Disease Control and the deputy minister. It met infrequently, usually twice a year. The Laboratory Centre for Disease Control, as its secretariat, organized meetings, prepared minutes and briefing materials, and generally took care of any business that needed to be addressed between meetings. The committee had no regulatory powers, indeed no power to do anything except give advice. Its resources, such as it had, were drawn from the resources of the Laboratory Centre for Disease Control.

In addition to playing a pivotal role for the National Advisory Committee on AIDS, the Laboratory Centre for Disease Control had its own resources for gathering information about AIDS. In the summer of 1984, its Bureau of Microbiology began testing for HIV antibody among high-risk groups. Dr Michael O'Shaughnessy of the bureau had trained at Dr Gallo's laboratory in Bethesda, Maryland, and there had learned the method of testing for HIV antibody. He also, while in Maryland, began testing blood samples that had been collected by Dr Christos Tsoukas for a study of immune abnormalities among a cohort of hemophiliacs in Montreal. On returning to Canada, Dr O'Shaughnessy developed a testing program at the Laboratory Centre for Disease Control, using a large quantity of antigen donated to the laboratory by Dr Gallo.

Antibodies that react against an invading organism are one of the body's defences against infection. Their presence usually indicates immunity that develops after infection. A common example occurs when a person is infected with measles as a child. The body, in fighting the infection, develops antibodies that remain for life, preventing a second infection. There are, however, exceptions to the general rule. Dr O'Shaughnessy and his supervisor, Dr Gill, were among those who believed that people who had the antibody to HIV were not immune but, on the contrary, were infected with the virus and would continue to be infected, and be infectious, for the rest of their lives. This life-long infectivity occurred because the virus was of a particular type – a retrovirus – that integrated itself into the genome, the part of the chromosome containing hereditary factors. Dr Gill and Dr O'Shaughnessy and their colleagues, including those employed by the Bureau of Biologics, regularly discussed these and other matters.

By August 1984, the Laboratory Centre for Disease Control was prepared to test blood samples submitted by the provincial laboratories for the presence of HIV antibody until commercial tests became available. The laboratory's Bureau of Microbiology established the following criteria, in order of priority:

- 1 Symptomatic individuals with AIDS or AIDS-Related Complex (ARC).

- 2 Individuals sustaining parenteral exposure to persons with AIDS, ARC, or who are positive for HIV antibody. This includes hemophiliacs, I.V. drug abusers, health care workers (needlesticks), and individuals who have received blood transfusions from persons who fit into one of the above three categories.
- 3 Individuals belonging to populations in which AIDS occurs with increased frequency and having evidence of AIDS-related immunological defects.
- 4 Cohabitants of individuals with AIDS or ARC or individuals positive for HIV antibody. This includes family members or partners residing in the same domicile.

Throughout the summer and autumn of 1984, disturbing data emerged from the testing program at the Laboratory Centre for Disease Control. In particular, it appeared that one-third of those Canadian hemophiliacs who showed no symptoms of AIDS were in fact antibody positive. At this time, the latency period between infection with the virus and development of AIDS was believed by most experts who accepted that HIV caused AIDS to be in the range of two to five years. (It is now believed that the latency period is much longer.) If the data were applicable to all persons infected with HIV, a large number of persons who were infected and could infect others would show no symptoms and would not know that anything was wrong. This possibility, serious in itself, was particularly troubling because many persons who gave blood were repeat donors and might give blood several times a year. The longer the latency period, the more donations an infective and unaware donor could make.

As noted in earlier chapters, the early stages of an epidemic can be likened to an iceberg. The part of the iceberg that is visible above the water-line represents the known and identified cases. The larger part of the iceberg that rests below the water-line represents unidentified infected persons. The longer the latency period of a disease, the greater the proportion of the iceberg below the water-line. Although it was not known precisely how big the AIDS iceberg was, staff of the Laboratory Centre for Disease Control recognized it was potentially enormous. Dr Gill, in particular, was clear in communicating the nature of the threat of AIDS – informing his superior, Dr Clayton, as well as Dr Albert Liston, the executive director general of the Health Protection Branch (later assistant deputy minister), and Dr A.B. Morrison, the assistant deputy minister. A memorandum dated 27 August 1984 from Dr Clayton to Dr Liston, drafted by Dr Gill, is striking in its stark portrayal of the threat of AIDS. Dr Clayton said that the hypothesis of Dr Gallo, that all those infected with the virus would go on to get AIDS, was tenable. He added:

There is, however, mounting evidence that this virus has already spread to the general public and that there is potential for an explosive outbreak in the next few years which will be impossible to stem without further understanding of the virus and its interaction with the human host ...

For all the foregoing reasons there is not only an opportunity, but an obligation for Canada to make a substantive contribution to understanding and controlling this disease. This contribution can be made most effectively by resourcing LCDC [Laboratory Centre for Disease Control] to respond to what may become the most serious scourge of mankind this century.

It was in this context of discussion and concern that the National Advisory Committee on AIDS, and the Laboratory Centre for Disease Control acting as its secretariat, considered the request from the Red Cross for help in dealing with the secondary issues surrounding the implementation of testing.

The most serious of these issues was the danger that persons might donate blood simply to learn their HIV status. One way to address this problem was to provide another way for persons to be tested that would be independent of the national blood system. For alternative test sites to be successful, however, they would have to be properly publicized and universally accessible without payment throughout the country. From the outset of discussions on HIV-antibody testing, the logical providers of alternative test sites were seen to be the provincial public health laboratories. These laboratories, which were an integral part of the provincial public health networks, were responsible for testing for other pathogens. Indeed, they were the only laboratories authorized to test for some sexually transmitted diseases. They were funded by the provincial governments and were within their jurisdiction and control.

Other issues surrounding HIV-antibody testing also distinguished it from other types of testing. One was that most persons with AIDS were homosexual men, a group subject to discrimination. Another was the terrible stigma carried by AIDS. Some persons called for a quarantine of those infected with the AIDS virus. An elected official in British Columbia proposed the creation of a special ghetto in Vancouver where all the gay population would be confined. It was even suggested that a former leper colony, Bentinck Island, be reactivated and that persons with AIDS and the gay population be confined there. In Nova Scotia there were calls for quarantine of gay persons on McNabs Island. Even though such extreme proposals were relatively rare, now that it was technologically possible to identify persons who had been infected by the AIDS virus there were, understandably, very serious concerns about what would be done with the information derived from the tests.

These issues, among others, were presented to the Ontario Human Rights Commission by the AIDS Committee of Toronto in June 1984 as part of a general brief:

AIDS AND BLOOD TESTS FOR HTLV-3/LAV

With the discovery of the probable cause of AIDS, the HTLV-3 or LAV virus, it appears that we are only a few months away from a blood test. These tests, however, will only show whether or not the person was once

exposed to the virus. It is not a test to see whether the virus is still in the person's body, whether they are infectious or even whether or not they will come down with AIDS or ARC [AIDS-related complex]. As with Hepatitis B, their bodies could have fought off the infection or they might be carriers. There will undoubtedly be controversial questions about how this information will be used, whether persons can be tested against their will or without their knowledge. For example, suppose a company requires a physical of every employee who participates in a medical insurance plan and one of the tests is for anti-bodies of HTLV. Potentially persons could be discriminated against on the basis of showing positive on this test without any evidence that they will come down with the syndrome or even be infectious.

These concerns were shared by many persons throughout the country.

The Red Cross took the position that the National Advisory Committee on AIDS should be involved in these matters in more than a merely advisory capacity, and that approval from that body would be a precondition for Red Cross implementation of testing for HIV antibody. On 14 September 1984, Dr Perrault told a meeting of the medical staff of the blood transfusion service that the Red Cross had been asked by a manufacturer to participate in test kit evaluations, but that use of any test would have to be endorsed by the National Advisory Committee on AIDS. Two weeks later, Dr Perrault wrote to the manufacturer and informed it that "the matter [of HIV-antibody testing] is being referred to the National Advisory Committee on AIDS as we will follow the recommendations of the national health authorities on the subject." He added that he was interested in comments made by the manufacturer that there were no regulatory restrictions on the distribution of kits in Canada and that he himself would discuss this point at the next meeting of the National Advisory Committee on AIDS.

Payment for HIV-antibody tests, as for all other aspects of the blood program, was to come from the provincial ministries of health, which were represented on the Canadian Blood Committee. Dr Martin Davey, assistant national director of the blood transfusion service of the Red Cross, testified that in the middle or third quarter of 1984, during discussions with the Canadian Blood Committee secretariat about the budget for the following year, he suggested that the costs of HIV-antibody testing be provided through a contingency fund of a few million dollars. He was told that the committee would not deal with the matter as a contingency fund, but as a supplementary budget when the costs could be defined. Former members of the Canadian Blood Committee who testified at the Inquiry confirmed that the committee did not provide for contingencies in its budgets for the Red Cross. However, during its consideration of the Red Cross's proposed 1985 budget, the Canadian Blood Committee had been alerted to the fact that HIV-antibody testing might be introduced in that budget year.

By this time, 21 September 1984, the first adult case of transfusion-associated AIDS had appeared in Canada. It was diagnosed by Dr Tsoukas at the Montreal General Hospital and reported to the Laboratory Centre for Disease Control, which in turn reported it to the acting assistant deputy minister in charge of the Health Protection Branch. This was not considered an "official" report. Despite its knowledge of the existence of this case, the Laboratory Centre for Disease Control, as well as the Red Cross, continued to state for months that there were no reported cases of transfusion-associated AIDS in Canada. In the United States at this time, sixty-nine adult cases of transfusion-associated AIDS and a further thirteen pediatric cases had been reported, and these, too, were known to the Laboratory Centre for Disease Control.

"Official" reports in 1984 were unreliable. The federal government had no power to require that diseases be reported to any authority. The channels for official reporting were through the provincial public health authorities, which were governed by provincial legislation. At the end of 1984, five provinces – Manitoba, Newfoundland, Nova Scotia, Prince Edward Island, and Quebec – still had not made AIDS reportable. The Laboratory Centre for Disease Control could expect no official reports from those provinces.

October 1984–January 1985: A Canadian study of HIV testing

Dr Perrault formally presented the issue of HIV-antibody testing to the National Advisory Committee on AIDS at a meeting on 9 October 1984. He suggested that the matter was sensitive and that a subcommittee should be developed to provide national guidance. The committee accepted this recommendation and undertook to strike an "ad hoc committee" or "mini task force" to review all aspects of the problems related to HIV-antibody testing. It was decided that "Canada should not introduce screening of blood or blood donors until the ad hoc committee reported back."

Dr Leclerc-Chevalier, executive director of the Canadian Blood Committee, attended that October meeting of the National Advisory Committee on AIDS. In December, she told her executive committee that during the coming year the Canadian Blood Committee might be asked to approve testing of blood for HIV antibody. She said the cost would be \$5 million, or \$10 million if two tests were conducted.

Three months after the National Advisory Committee on AIDS recommended the establishment of a task force on HIV-antibody testing, no steps had yet been taken to create one. Not until 9 January 1985, when the matter came before the committee's epidemiology and public health subcommittee, was a chair, Dr Mathias, chosen as an initial organizing step.

In the United States, the Food and Drug Administration and the blood-banking industry had been moving quickly towards the implementation of HIV-antibody testing. A number of studies had been conducted in the autumn

of 1984 on the extent to which persons at high risk of contracting AIDS reacted positively to HIV-antibody tests. The results were published by the Centers for Disease Control in Atlanta in its journal, the *Morbidity and Mortality Weekly Report*, on 11 January 1985. They were alarming. Data from several studies showed that between 22 and 65 per cent of homosexual men were antibody positive, as were 87 per cent of intravenous drug abusers and 56 to 72 per cent of persons suffering from hemophilia A. Moreover, HIV itself had been isolated from 85 per cent or more of the persons who tested positive for the HIV antibody – making clear that the presence of antibody was indicative of infection and infectiousness. The studies also revealed that viremia, the condition in which the presence of virus in the blood causes a person to be infectious, could persist for years whether or not the person suffered from any symptoms.

By this time, manufacturers had developed test kits that would soon be licensed. The 11 January 1985 issue of the *Morbidity and Mortality Weekly Report* also contained recommendations from the U.S. Public Health Service that all blood and plasma donations be tested for HIV antibody. Three days later, on 14 January, the Public Health Service convened a meeting to consider those recommendations. Representatives of the American Red Cross, the Council of Community Blood Centers, and the American Association of Blood Banks attended. On the next day, 15 January, the national headquarters of the American Red Cross told its local blood services that it was negotiating purchase agreements for test kits; as soon as one or more kits became licensed and available, it would issue a directive requiring testing of all blood donations. Representatives of the blood-banking industry met officials of the U.S. Food and Drug Administration on 17 January to discuss the industry's concerns about the implementation of testing. Among those concerns were the need for well-publicized alternative test sites, the means of informing donors of test results, and the need for donors' consent to testing.

In light of the speed at which matters were proceeding in the United States, the value of a Canadian task force that had yet to be organized was questionable. In a letter to the Laboratory Centre for Disease Control on 11 January 1985, Dr Mathias asked for its help in organizing the task force he chaired, and said that, in view of the imminent release of test kits in the United States, it was important that the task force be prompt in meeting the needs of the Red Cross. He also raised the question whether the task force was still needed. Senior members of the laboratory centre considered this question and concluded, in an internal memorandum dated 17 January 1985, that

there has to be a Task Force. The reason is that NACAIDS has said there should be one, and further that NACAIDS has agreed that HTLV-III screening of blood donors in Canada should await the report of this Task Force.

The task force was organized. Its first meeting was scheduled for 7 March 1985.

At the end of January, more than 250 representatives of blood-banking and governmental organizations attended a two-day meeting organized by the American Blood Commission and the Hastings Center Institute of Society, Ethics and the Life Sciences at Arlington, Virginia. The purpose of the meeting was to discuss the implementation of HIV-antibody testing and the related issues and problems. Dr Derrick of the Red Cross and Dr Norbert Gilmore, chair of the National Advisory Committee on AIDS, attended. Important data about the prevalence and significance of HIV infection were presented and discussed. They included statistics showing that between one in two hundred and one in a thousand U.S. blood donors were confirmed to be HIV-antibody positive. The participants agreed that testing should begin as soon as kits were available. However, since alternative test sites and counselling services would not be available in all locations immediately, it was also agreed that, during an interim period, donors would not be notified of test results so as to discourage persons at high risk from donating blood or plasma as a way of determining their status.

The Hastings Conference also decided that the donor-screening measures being used in the United States should remain in place. This was essential because it was not known how many infected individuals would test negative ("false negatives") or how long the "window period," during which a person was infected but did not yet test positive, could persist. Until HIV-antibody testing could begin, rigorous and effective donor screening was universally recognized in the blood-banking industry as the principal means of protecting the blood supply from HIV.

On 19 February 1985, the U.S. Food and Drug Administration sent a letter to all U.S. blood-banking establishments, designed to answer questions that would accompany the implementation of HIV-antibody tests. The letter said that test kits would be licensed soon and directed that laboratories immediately begin to purchase the necessary equipment and train personnel to perform the tests.

February 1985: Evaluation of test kits

Meanwhile, in Canada, the Red Cross was preparing to evaluate a commercially produced ELISA test kit provided by Abbott Diagnostics of Chicago. At that time, a number of manufacturers had tests at various stages of development. The final stage in any test development is field evaluation, involving a large number of samples. Other evaluations of the Abbott test kit were being performed in the United States and Australia. Subsequently, in all three countries the conclusion was reached that the Abbott test kit was either the preferred kit or one of several acceptable kits. The American Red Cross and Canadian Red Cross eventually purchased the Abbott kit.

The Canadian Red Cross evaluated the Abbott test kit at the national reference laboratory between 5 and 19 February 1985. This was the same kit that was licensed in the United States at the beginning of March and ultimately used in Canada. Three thousand samples were collected from the Toronto centre. These samples were "unlinked," that is, the donors from whom these samples were taken could not be traced or otherwise identified. Eleven of them were found to be "repeat reactive," meaning that they twice tested positive on ELISA tests. Ten of the eleven were confirmed positive by the western blot test, carried out by Abbott Diagnostics in Chicago. At the time, western blot tests were not standardized or as reliable as they later became. In April 1985, Abbott released revised results. Only eight samples were confirmed positive.

Since the samples were unlinked, the Red Cross was unable to remove the HIV-antibody positive donations from the blood supply, or to tell the donors of their positive status or prevent those donors from donating again. The Red Cross was also unable to initiate look-backs to determine who might have received transfusions or blood products from those donors in the past.

It is not clear why the evaluation of the Abbott test kit took place with unlinked samples. Dr Davey, the assistant national director of the Red Cross blood transfusion service, testified that it was a condition of the contract with Abbott. However, the Red Cross, despite requests, could not produce a copy of a contract documenting such a condition. On the contrary, statements made by Dr Davey at the November 1984 meeting of the blood transfusion service advisory committee suggest that it was the Red Cross that decided to use unlinked samples from the outset. The minutes of that meeting state:

Dr Davey said that to date the CRCS BTS [Canadian Red Cross Society Blood Transfusion Service] has been approached by three of the five suppliers of AIDS test kits to look at their test material. No decision will be made until further discussions have taken place. It may be decided to test some uncoded and non-identifiable specimens in order to get some experience with the test and also to obtain some preliminary information of the percentage of antibody-positive Canadian blood donors.

Dr Davey testified that with an unlicensed test, as the Abbott test was at the time, the Red Cross preferred to evaluate it with unlinked samples. He said that this was also the practice in phase II evaluations of the same test kit in the United States.

March 1985: Licensing of test kits in the United States; recommendations for action in Canada

On 2 March 1985, five days before the National Advisory Committee on AIDS task force was scheduled to meet, the U.S. Department of Health and Human Services approved screening tests for HIV antibody. Test kits began to move

to blood banks in the United States immediately. This fact was reported in the media, including the Canadian media. Two days later, Dr Perrault sent a telexed message to the board of directors and medical directors of the Red Cross to assist them "in responding to media enquiries." It included the following information:

The decision to test blood donors for AIDS is the responsibility of the Department of [National] Health and Welfare, which will consider recommendations from the National Advisory Committee on AIDS and its special task force on AIDS testing;

The Canadian Red Cross Society, represented on the National Advisory Committee on AIDS and the task force on AIDS testing, will be making its recommendations through those bodies;

The Canadian Red Cross Blood Transfusion Service National Reference Laboratory is currently evaluating the test kits supplied by U.S. manufacturers. A report will be submitted to the health authorities concerning the reliability of the test and the feasibility for use in the blood transfusion service;

As in the U.S., the Red Cross acknowledges that the test is fallible and may cause undue concern in blood donors who would require to be informed of the results of the test;

Contrary to the American situation, there have been no officially-recognized cases of transfusion-associated AIDS in Canada to date, so the success of the screening programme would not be immediately visible;

Depending on the results of the National Reference Laboratory evaluation, and the availability of kits, it is not anticipated that donor testing will be possible before the second half of 1985. Uniform testing across the country could be further delayed for logistic reasons.

The content of this message was incorporated into a briefing document for the Minister of National Health and Welfare prepared by the Canadian Blood Committee secretariat on 6 March 1985.

It is significant that the Red Cross took the position that it was the responsibility of the Department of National Health and Welfare to decide whether to test blood donors for AIDS. In testimony at this Inquiry, senior officials of that department disagreed. Dr Clayton, the director general of the Laboratory Centre for Disease Control, testified that "[i]n no way whatsoever ... was ... [the decision whether to test blood donors for HIV] the decision or responsibility of the Department of [National] Health and Welfare." Dr John Furesz, the director of the Bureau of Biologics, testified that the bureau had no control over screening procedures or the implementation of testing. Similarly, Dr Liston, the assistant deputy minister in charge of the Health Protection Branch, testified that it was not the responsibility of the Department of National

Health and Welfare to decide whether blood donors should be tested. In the United States, the Department of Health and Human Services and the Food and Drug Administration took an active role in regulating the blood supply and requiring testing when it became appropriate. In Canada, the Department of National Health and Welfare did not regulate the donation and distribution of blood and blood components until 1989. It did, however, regulate the collection of plasma by plasmapheresis and, indeed, required that such donors be tested regularly for syphilis and that every unit of plasma be non-reactive to a test for hepatitis B.

Dr Perrault's message to the board and medical directors also repeated the statement that there were no "officially-recognized cases of transfusion-associated AIDS cases in Canada" and that the success of the program would therefore not be immediately visible. While technically accurate, this statement obscured the fact that, as previously pointed out, unofficial transfusion-associated AIDS cases were beginning to surface.

When the National Advisory Committee on AIDS task force met on 7 March 1985 in Ottawa, the participants included Dr Davey of the Red Cross; Dr Gill, Dr O'Shaughnessy, and Dr Clayton of the Laboratory Centre for Disease Control; Dr Furesz of the Bureau of Biologics; Dr Gilmore of the National Advisory Committee on AIDS; and Dr Leclerc-Chevalier of the Canadian Blood Committee. The task force included no members of the provincial public health departments.

The meeting was provided with the latest clinical and epidemiological information about AIDS. Data from Dr Gallo's group in the United States showed that 70 per cent of homosexual men who tested positive for HIV antibody but showed no symptoms of infection were shedding virus and were therefore infectious. The minutes of the meeting recorded the working hypothesis that all positive samples were to be considered infectious:

A positive test result can only be interpreted to mean the individual has been exposed to the virus. Since virus has been isolated from a large number of asymptomatic antibody-positive individuals (70% of homosexuals in one study), all positive blood samples should be considered infectious. A negative test result does not mean that an individual is non-infectious, since persons with viremia may be antibody-negative, and newly infected individuals may remain seronegative for 6 months or more.

Data were also presented on the prevalence of HIV antibody among blood donors. In U.S. data from the Centers for Disease Control, 1 per cent of donors tested reactive on an initial ELISA. One half of these were reactive on a repeat ELISA, and of these 60 per cent were confirmed positive by western blot. In other words, the Centers for Disease Control data indicated that three out of 1,000 blood donors could be infected with HIV. Additional data from

the U.S. had found that of 60,000 serum samples, 1 per cent were reactive on initial ELISA and 0.6 per cent (approximately 360) were repeat reactive. Preliminary Canadian data were similar. The Red Cross's national reference laboratory reported that of 3,000 samples tested in the course of the evaluation of one test kit, 0.4 per cent were reactive in a repeat ELISA test.

No data were presented to the task force about the effectiveness of Canadian efforts to prevent persons at high risk of contracting AIDS from donating blood. However, Dr Davey reported that Red Cross donor-screening policies "had not had a major effect on the number of blood donors and, although unable to systematically evaluate its effectiveness, the general impression was that the system is effective." There was no indication in the minutes of the meeting of the basis upon which this general impression was drawn.

Dr Perrault testified, however, that it was believed that homosexual men represented between 4 and 10 per cent of the population and had previously donated at the same rate as heterosexual donors. If the belief was correct and screening had been effective at preventing homosexual donors from donating, one might have expected that there would have been a noticeable effect on the number of blood donors.

By the end of the 7 March meeting, the task force had drafted a number of recommendations. The most important were that all blood and plasma donations should be screened for HIV and that the Red Cross should develop an implementation plan and report to the National Advisory Committee on AIDS by 30 April 1985. The task force also recommended that the Canadian Blood Committee and the Department of National Health and Welfare determine with the Red Cross what resources were necessary to implement testing.

The recommendations of the task force went through a series of drafts after the meeting, incorporating changes suggested by the Red Cross. The fourth and final set of recommendations was approved and circulated to the National Advisory Committee on AIDS and those groups to whom the recommendations were directed before the committee met on 15 May 1985. The recommendations were in two parts; the first related to "screening," the second, to "diagnostic applications." The distinction recognized that the test kits were designed for screening rather than diagnosis. With their high sensitivity and low specificity, they could be expected to identify the vast majority of infected and infective persons. They would also, however, identify as reactive a large number of persons who were not in fact positive. They were thus a poor diagnostic tool.

One recommendation of the task force was implemented rapidly. It was that the Bureau of Medical Devices, part of the Health Protection Branch of the Department of National Health and Welfare, evaluate all HIV-antibody test kits and that no kits be distributed in Canada until the evaluation had been completed and reported to the National Advisory Committee on AIDS. Within a week, on 12 March, the Health Protection Branch told all known

manufacturers of test kits that evidence of the effectiveness of the products would have to be submitted if the products were to be sold in Canada.

The kits concerned had already been licensed by the Food and Drug Administration in the United States on 2 March 1985. The Bureau of Medical Devices had never previously regulated test kits for other diseases, nor did it have the laboratory resources to evaluate HIV-antibody test kits. It became involved because of the possibility of HIV-antibody test kits being misused as a diagnostic tool. Regulation by the Bureau of Medical Devices was a means by which the Health Protection Branch could monitor and control the use of the test kits for this purpose. The laboratory evaluations were, in fact, carried out by the Laboratory Centre for Disease Control, which measured the effectiveness of the tests against a panel of known samples. Evaluation of the first two kits, including the Abbott kit, was completed by 28 May 1985. The manufacturers were told the kits could be distributed in Canada.

On 22 March 1985, Dr Clayton wrote to provincial laboratory directors throughout the country about the need for alternative test sites. He said the sites would be "essential to deter ... persons from using the Canadian Red Cross as a diagnostic facility" and that provinces would need to train persons to perform the test and to develop educational materials for those who tested positive.

April 1985: The Red Cross's plan for testing

At a meeting of its medical directors on 27 and 28 March 1985, the Red Cross decided that testing should proceed, even if alternative test sites were not in place. As at the Hastings Conference in the United States two months earlier, the Canadian medical directors decided that donors would not be notified of their test results until alternative test sites became available.

The Canadian Blood Committee's executive committee met on 17 April 1985. Dr Leclerc-Chevalier, the executive director, reported that the task force had met and that the Red Cross had been asked to develop an implementation plan for HIV-antibody testing. There appears to have been no discussion about the task force recommendation that the Canadian Blood Committee and the Department of National Health and Welfare determine with the Red Cross what resources would be needed. Resources were mentioned only in the context of a Red Cross position paper outlining additional staff needed to maintain a "watching brief" on the developing knowledge about AIDS and to participate in committees and correspond with organizations concerned with AIDS and blood issues. The watching brief was not a new idea; the Red Cross had been carrying out such monitoring since 1982. The executive committee told Dr Leclerc-Chevalier to determine whether additional positions were required to carry out these functions or whether the current Red Cross budget and personnel were sufficient.

Although the executive committee was not specifically called upon to assist in the implementation of testing, it had before it material that explained the need for action. The Red Cross position paper stated:

Development[s] in the U.S. which culminated in the implementation of HTLV-III [HIV] antibody testing on March 2, 1985, could not be foreseen at the time of the 1985 budget preparation (in August 1984). The subsequent pressures placed on the National Health Authorities and the CRCS in Canada have given a new focus and urgency to the initiation of HTLV-III antibody testing to screen out possibly infectious blood.

Members of the Canadian Blood Committee testified that it was their view at that time that the matter was being considered by other organizations such as the Red Cross and the National Advisory Committee on AIDS and that there was a process in place to bring about the implementation of testing.

Nothing before the Canadian Blood Committee executive committee at this April meeting suggested that it consider ways to expedite approval of funding for HIV-antibody testing. Members were not asked by the executive director to prepare to authorize the additional expense of HIV-antibody testing or to find some means of circumventing the normally cumbersome and time-consuming process of budget approval by twelve provincial and territorial governments.

The members of the committee needed help to understand the nature of the problem they were facing. Almost all the members were administrative and financial officials from provincial governments. Their responsibilities on the Canadian Blood Committee represented a small proportion of their ordinary work. They were not public health officials, and their training and experience did not qualify them to recognize an urgent public health problem without assistance. They depended upon others, particularly their executive director, to be their eyes and ears and to bring important scientific information to their attention. Under these circumstances, one would have expected that the executive director, who had been present at the National Advisory Committee on AIDS task force meeting of 7 March 1985, and who testified that she recognized the urgency of the situation, would have given her members advice about what the Canadian Blood Committee should do to facilitate an expeditious beginning of testing.

Testing was discussed at a meeting of the Red Cross blood transfusion service advisory committee on 26 April 1985. Dr Leclerc-Chevalier attended, as did Dr Alfred Katz, a senior official with the national office of the American Red Cross. He reported that to that date in the United States 0.23 per cent of donors had been found to be HIV-antibody positive. David Balfour, the president of the Canadian Red Cross, expressed the view that "immediate

action was indicated." Dr Perrault responded that he agreed and that it could be expected that the National Advisory Committee on AIDS would be making a recommendation for implementation of testing as soon as possible after it met on 15 May.

Concern was expressed at this advisory meeting that if alternative test sites were unavailable, donor clinics would be overwhelmed with "high-risk" persons seeking diagnosis. Dr Davey testified that at the time of the meeting he was reasonably satisfied that this concern could be answered by a policy of non-notification. He also testified, as did Dr Perrault, that they and Mr Balfour believed that testing ought to begin as soon as possible after the National Advisory Committee on AIDS meeting on 15 May. The blood transfusion service advisory committee recommended that testing proceed, subject to the approval of the Red Cross board of directors. Dr Perrault was asked at the hearings why the issue of HIV-antibody testing had to be brought to the board of directors, which consisted for the most part of lay persons. He conceded that it would have been improbable that the board would come to any conclusion different from the recommendation, but that it was necessary, nevertheless, to bring the matter to the board before going to the Canadian Blood Committee.

As directed by the task force, the Red Cross prepared an implementation plan for testing, which it provided to the secretariat of the National Advisory Committee on AIDS on 1 May 1985. Its proposed timetable follows:

- | | |
|--------------------------------------------------------------------------------------------------|-------------------------------------------------|
| 1. Test kit evaluations begin,
to be completed by | February 1985
mid-May 1985 |
| 2. Request to Bureau of Medical Devices
to allow supply of U.S. licensed kits to
Red Cross | April (done) |
| 3. Request to supplier for quotation | April
(done/received) |
| 4. Budget presented for approval | May |
| 5. Budget approved | Canadian Blood
Committee,
before 30 June? |
| 6. Centres to start hiring staff | July |
| 7. Contract signed with supplier | July |
| 8. Training of blood centre staff in Toronto | July–August |
| 9. Implementation of screening | August |

10. Subsequent interval before Red Cross can supply	
- all red cells screened	3-5 weeks
- all plasma/cryoprecipitate screened	+ 5-12 weeks
- plasma fractions only from screened plasma	6-9 months

May 1985: Preparations for implementation; involvement by the provinces

On 6 and 7 May, a meeting was held of the technical advisory committee for laboratory services, a committee made up of provincial public health laboratory directors from all parts of Canada. The committee members were informed of the Red Cross implementation plan and the need for alternative test sites. They recommended that the Minister of National Health and Welfare suggest to provincial health ministers that they designate appropriate laboratories in their provinces for HIV-antibody testing.

The National Advisory Committee on AIDS met in Ottawa the next week, on 15 May. Several motions on the matter of HIV-antibody testing were passed, including the following:

- the recommendations of the task force be accepted and forwarded to the Minister of National Health and Welfare
- the Red Cross implementation plan be accepted
- the recommendation of the technical advisory committee for laboratory services be endorsed
- a further task force of the National Advisory Committee on AIDS study the implications and implementation of alternative test sites
- HIV-antibody test kit makers be informed that there was no objection to the supply of test kits in Canada for the purpose of screening blood donations

A later study of donors in the United States, following the start of testing there, found that donations were still being received from persons who should have been deferred by standard donor-screening techniques. In fact, all donors who tested positive in the United States were members of high-risk groups. At this time, the Canadian risk-reduction measures were less stringent than those in place in the United States.

Following the meeting of the National Advisory Committee on AIDS, two parallel processes took place involving provincial officials. One concerned funding for HIV-antibody tests. The other involved the federal government in explaining to provincial governments their role with respect to alternative test sites.

The request for funding came officially on 17 May 1985, when the Red Cross sent the Canadian Blood Committee a detailed budget for its HIV-antibody testing plan. The committee received the budget on 21 May 1985.

The information was not sent to the committee earlier, not because it was unavailable but because the Red Cross felt obliged to wait until the National Advisory Committee on AIDS meeting had taken place. Dr Perrault testified that the Red Cross felt it would have been "questioned on that" and that an earlier submission "would have been seen as pre-empting discussion." The Red Cross estimated that the cost of testing for the remainder of 1985 would be \$2.6 million and for all of 1986, \$5.5 million. This budget was put on the agenda of the next scheduled Canadian Blood Committee meeting, on 4 and 5 June 1985. It was not given to Canadian Blood Committee members in advance, nor were members of the Canadian Blood Committee asked to come to the meeting with approval in hand from their respective governments to fund the testing program.

Communications between the federal and provincial health ministries with respect to alternative test sites took a circuitous route. After the National Advisory Committee on AIDS meeting, the recommendations were forwarded to the deputy minister and Minister of National Health and Welfare. Three recommendations were addressed specifically to the Minister: first, that he inform provincial ministers of health about the need to set up alternative test sites; second, that he ask ministers of health in provinces that had not already made AIDS a reportable disease to do so; and third, that additional federal resources be given to the Laboratory Centre for Disease Control to "continue to manage AIDS at the national level."

June and July 1985: Delays in funding

The Red Cross anticipated a speedy budget approval by the Canadian Blood Committee. Under its anticipated schedule, testing was to start on 9 September 1985. A two-day training session in Toronto, for staff responsible for testing at the seventeen blood centres, was planned for 29 and 30 July, and accommodation was booked.

The issues involved in HIV-antibody testing were presented to the Canadian Blood Committee on 4 and 5 June 1985. Senior Red Cross officials, including Dr Perrault and Dr Derrick of the blood transfusion service, attended, as did Dr Gilmore of the National Advisory Committee on AIDS. Dr Gilmore outlined the seriousness of the threat of AIDS to the blood supply. The recommendations of the National Advisory Committee on AIDS and the Red Cross's implementation plan were presented. Members of the Canadian Blood Committee asked about a number of matters, including the desirability of testing blood donations before alternative test sites were in place. The representatives of both the Red Cross and the National Advisory Committee on AIDS said testing should take place as soon as possible, whether or not alternative sites were operating. An in-camera meeting of the committee members followed, during which it was suggested that the secretariat look at the proposed budget and monitor actual expenditures to ensure that the money was

really being spent on AIDS. The chair observed that there was probably enough money to deal with cash flow problems, but that what was needed was an "agreement in principle" subject to individual members' clearing the issue with their own governments and securing a high priority for the matter at the provincial level. A motion was passed

approving in principle that the CRCS continue to plan for the implementation of the testing of blood and plasma donations for AARV [HIV] antibodies, at an appropriate time, subject to review of the proposed budget by the CBC Secretariat and subject to consultation with provincial departments of health, with final approval to be given by June 30, 1985.

The motion's deadline, 30 June 1985, was the latest date the Red Cross had projected in its implementation plan for approval by the Canadian Blood Committee. Dr Gilmore testified that, in retrospect, he was "astonished" that the implementation plan had not been approved and the authorization given immediately.

Although both the Red Cross and the National Advisory Committee on AIDS had recommended that testing of blood samples proceed as soon as possible, even if alternative test sites were not yet available, the Canadian Blood Committee representative from Ontario was not convinced. On 6 June 1985, the day after the committee met, he wrote to the director of his province's Public Health Branch:

If the Red Cross is provided with budget approval by the end of June, they estimate that they could commence testing by the end of August.

However, as you are aware, there are a number of important issues that have to be settled before anyone should feel comfortable approving the funding for the Red Cross testing program. Having said this, though, the inevitability of the testing program as a way of reassuring the public that Canada's blood system is free of AIDS must be recognized ...

Fundamental questions include:

- 1 When should the Red Cross introduce its donation testing program?
- 2 When should provinces introduce alternate site (public health) testing of the public?
- 3 Should implementation of 1 and 2 be simultaneous, and should provincial testing be simultaneous in all provinces?
- 4 Should the Red Cross be advising donors of the results of screening their blood donation? This question has social, ethical, legal and medical ramifications.

With respect to the committee's 30 June deadline for "final approval," he wrote:

Because of the growing public concern about the spread of AIDS, which will increase as more and more cases are reported in the media, it was decided that the individual members of the Canadian Blood Committee would attempt to obtain an indication of where their Ministry/department stood on the question of providing the additional funding required by the Red Cross, by the end of June.

Dr Evelyn Wallace, senior medical consultant with the Ministry of Health in Ontario, responded to these questions on 17 June. She said it was imperative that the Red Cross be funded and that testing be initiated, and that, "ideally," alternative test sites should be in place when Red Cross testing began.

A week earlier, on 10 June 1985, Dr Leclerc-Chevalier had clarified the meaning of the Canadian Blood Committee's motion. She wrote two letters to the Red Cross, one to George Weber, the secretary general, and the other to Dr Perrault. Dr Leclerc-Chevalier told Mr Weber that the Canadian Blood Committee was "not in a position to approve donation testing until federal and provincial authorities ... had an opportunity to discuss issues such as alternative testing sites, testing for diagnostic purposes, information to donors, patients and health workers, etc." In her letter to Dr Perrault she concluded that "at the present time, no additional resources have been approved by the Canadian Blood Committee."

Dr Perrault testified that he had understood the "approval in principle" of the Canadian Blood Committee to mean that the Red Cross could only continue planning, but that by this time there was no more planning to do. They could do no more without approval of funding. At this time, the Red Cross had a budget surplus from 1984 of approximately \$2.3 million, nearly as much as its estimated budget for testing for the remainder of 1985. Nevertheless, the Red Cross did not seriously consider financing testing from its own funds before receiving approval from the Canadian Blood Committee.

Members of the Canadian Blood Committee who testified at the Inquiry said they had intended their approval in principle to mean that the Red Cross could continue not only to plan, but also to commit the resources necessary to continue with its implementation plan. They expected that Red Cross planning would proceed concurrently with the Canadian Blood Committee's process of funding approval. All agreed that the Red Cross would have been well within its rights to commit funds for necessary expenses such as training of staff members.

Mr Weber testified that he believed that the Canadian Blood Committee, in its 10 June letter to him, had told the Red Cross not to go ahead with testing. He replied a week later, stating that the Red Cross understood "the Provinces' requirements to discuss issues surrounding the AIDS problem." In particular, he acknowledged that the provinces needed to discuss the issues

of alternative test sites, testing for diagnostic purposes, and information to "donors, patients, and health care workers" before they could make a final decision on funding testing.

The Canadian Blood Committee's financial analyst, Randall Klotz, did not begin reviewing the Red Cross budget until after the meeting that ended on 5 June. He completed it on 27 June, and provided the results to committee members on 2 July. No one had asked him to begin his review before the meeting.

Meanwhile, federal and provincial consultations continued. On 12 June, David Kirkwood, deputy minister of the Department of National Health and Welfare, sent a telexed message to provincial and territorial ministers of health inviting them to a meeting on AIDS to discuss resolution of problems associated with implementing HIV testing. The issues included testing for diagnostic purposes, the availability of alternative test sites, the confidentiality of test results, and the responsibility for informing donors of test results. On 14 June 1985, a briefing note prepared for the Minister of National Health and Welfare by the Canadian Blood Committee secretariat predicted that the provinces would approve funding for the Red Cross plan by the end of the month. It explained that the delay in arriving at a final decision resulted from problems associated with implementation of the test. These were expected to be resolved at the federal-provincial/territorial meeting, scheduled for 28 June. In fact, the meeting was not held until 4 July. On 30 June, Dr Leclerc-Chevalier told Mr Weber that the Canadian Blood Committee would not be able to give its approval until approximately one week after that date.

The decision to withhold funding approval until after 4 July was first discussed within the Canadian Blood Committee by Dr Leclerc-Chevalier and Ambrose Hearn, the committee's chair. Mr Hearn suggested that Dr Leclerc-Chevalier discuss the question with other members. A final decision to delay the approval was reached on 24 June at a meeting of the committee secretariat.

On 26 June, Fred Anderson, the representative from Manitoba, told Dr Leclerc-Chevalier that, unless he notified her differently by 12 July, Manitoba would agree with the decision of the other members of the Canadian Blood Committee about the funding of HIV-antibody testing.

On 27 June, Mr Hearn sent a telexed message to all provincial ministers of health, informing them of the state of funding approval and the Canadian Blood Committee's position. He said that the committee had supported the Red Cross proposal in principle and had asked the Red Cross to continue planning while the committee reviewed the budget and consulted with provincial ministries about the integration of HIV-antibody testing into their own programs. The message continued:

Committee members felt it would be inappropriate to give final approval to the testing of donations, until such time as federal and provincial health ministries have discussed related items such as: alternative testing sites,

testing for diagnostic purposes, provision of information on test results and, sociological, ethical, legal and medical concerns. The Canadian Blood Committee felt that these items are beyond its mandate which relates to the Canadian blood system and more specifically on the AIDS issue, to the safety of the Canadian blood and blood product supply.

When the federal-provincial meeting on AIDS was held in Ottawa on 4 July, all provinces except British Columbia and Prince Edward Island were represented. The territories were not represented. The primary purpose of the meeting was to deal with the issue of alternative test sites. Elaine Boily-Nichol, program analyst of the Canadian Blood Committee secretariat, attended, as did Dr Davey and Dr Derrick on behalf of the Red Cross. Several of the provincial representatives were also members of the Canadian Blood Committee. Most of the provincial representatives, however, were epidemiologists and persons involved in the management of provincial laboratory services. No provincial deputy or assistant deputy minister attended. Dr Davey testified that their absence caused the Red Cross concern; it meant that the meeting could not reach decisions and would result only in participants returning to their provincial ministries with proposals for approval. The minutes of the meeting, however, reveal no expression of concern about delay on the part of the Red Cross. The meeting supported the Red Cross's view that its responsibility lay in ensuring the safety of blood supplies, not in the diagnosis of donors or the provision of counselling or other services for persons with AIDS or HIV.

The National Advisory Committee on AIDS argued in its report to the meeting that alternative testing "must be available" when the Red Cross began testing. This was an apparent change in position since its 15 May meeting and the Canadian Blood Committee meeting of 4 and 5 June. In his testimony, Dr Gilmore explained that the National Advisory Committee on AIDS had viewed the federal-provincial meeting as a gathering with the sole objective of bringing people together to talk about alternative test sites. He said he had sensed that the idea would meet resistance and was trying to get the participants to move further towards agreement.

In his presentation to the meeting, Dr Davey discussed the value of both heat treating coagulation factor concentrates and HIV-antibody testing as measures to reduce the threat of transfusion-associated AIDS. He said that even if heat-treated factor concentrates had been available in the previous five years, "only three AIDS cases would have been prevented at this time." He quoted the same figure for HIV-antibody testing:

Had this type of testing been available to the CRCS [Canadian Red Cross Society] in the past 5 years, only three cases of AIDS would have been prevented at this point in time. Future activities of this type by the CRCS may reduce the numbers of AIDS cases reported by the order of only 1-2%.

In his evidence, Dr Davey rejected a suggestion that these comments were intended to minimize or understate the significance of heat treatment and HIV-antibody testing. Rather, they were made, he said, to demonstrate that the "Red Cross [was] putting substantial resources into control of AIDS."

Dr Davey also told the federal-provincial meeting that the Red Cross had received approval in principle from the Canadian Blood Committee for its testing plan, but "[had] been asked to place the program on 'hold' until the request [had] been examined in detail and the program [had] been funded." There is nothing in the minutes of the meeting to suggest that the members of the Canadian Blood Committee who attended the meeting disputed Dr Davey's characterization of the meaning of the committee's approval in principle.

The summary of agreements and recommendations of the meeting records that the provinces agreed to establish alternative test sites and that full implementation of HIV-antibody testing of blood donations would likely not occur until twelve weeks from the date of formal approval by the Canadian Blood Committee.

On 5 July 1985, the day after the meeting, the Canadian Blood Committee's secretariat told the Red Cross that it would receive the decision on resources for AIDS screening by 12 July. On 11 July, officials of the Red Cross, including Dr Davey and Dr Derrick, met with Ms Boily-Nichol, who had represented the committee's secretariat at the federal-provincial meeting. Dr Derrick expressed concern about the delay in providing the Red Cross with funding approval. He also emphasized "the importance of mentioning, in the letter of approval to the Red Cross, that the screening of blood donations would be implemented in conjunction with the setting up of alternative test sites."

By 12 July, all the provinces except Ontario and Manitoba had indicated their approval of the implementation plan. The Ontario Ministry of Health sought approval from the provincial Management Board on 15 July. The Manitoba representative to the Canadian Blood Committee had stated that his province would follow the decision of the other provinces, but on 30 July, upon returning from vacation, he told the committee that Manitoba had not yet approved funding because not all the other provinces had yet made a decision. Ontario's approval was announced on 1 August. Manitoba followed on the same day.

Before the federal-provincial meeting on 4 July 1985, the Red Cross had planned a training workshop on HIV-antibody testing to be held on 29 and 30 July. The choice of these dates was premised on funding approval by the end of June. When it became apparent that funding would not be approved before 12 July, the Red Cross postponed the training workshop indefinitely. The members of the Canadian Blood Committee who testified said they were unaware of the postponement until they appeared at the hearings. Mr Hearn

said he was "astounded" to learn of this. Ultimately, the training session was held on 23 and 24 September, almost two months later.

The Red Cross continued to express its concern over the delay in approval. On 15 July, Mr Klotz, the financial analyst on the Canadian Blood Committee secretariat, summarized a conversation with Dr Derrick:

Dr Derrick, as he did last week, expressed his concern on timing and growing pressure from users and the press. I did not mention the issues developing regarding Ontario's position, that is, the annoyance with CRCS information to the media, the timing for Management Board approval – 2 to 3 weeks – and the fact that Ontario would prefer to delay the CRCS commencement to allow the diagnostic side of AIDS to be readied in the province.

Meanwhile, at the Royal Victoria Hospital in Montreal, testing of blood components for HIV antibody was taking place. Dr Gilmore, who practised medicine at the Royal Victoria, testified that the hospital had access to the test kit and used it, but kept the fact secret out of concern that "as soon as the word got out that blood was being screened, the hospital would get overwhelmed."

August 1985: Approval of funding

On 1 August 1985, the Canadian Blood Committee notified the Red Cross that its plan and budget had been approved. The same day, Dr Derrick sent a telexed message notifying members of the Red Cross that testing would begin within twelve weeks. On 12 August, Dr Davey told the senior Red Cross blood transfusion service personnel that funding had been approved and explained the reason for the delay as follows:

Prior to the approval of the implementation plan, there had to be a considerable amount of consultation with all levels of government and health departments. We are sorry, but not responsible, for the delay that has occurred. We are now, however, starting testing with full approval of the NACAIDS, the Provincial and Federal Ministries of Health, and the Canadian Blood Committee. In addition, the Canadian Red Cross has the unique opportunity of commencing testing uniformly across the country in parallel with the introduction of diagnostic tests for AIDS by all provincial Public Health Services.

Dr Davey wrote that screening of all incoming donations would start in the days after the training workshop, and that hospitals would be provided with only screened blood and blood components after 1 November 1985. Plasma

fractions from screened plasma would follow six to nine months later. These objectives were met.

Alternative test sites

During the federal-provincial meeting on 4 July 1985, a consensus was reached that alternative test sites be established and that testing be universally available, easily accessible, and free of direct cost to the person tested. One of the principal purposes of these test sites was that persons at high risk of contracting AIDS, who might otherwise donate blood in order to learn whether they were infected with HIV, would be able to obtain a test confidentially, with ease and at no expense. Every province was asked to designate at least one laboratory that would be capable of providing both ELISA and confirmatory testing. A person wishing to be tested would go to his or her physician or to a clinic where a blood sample would be taken and sent to the designated laboratory. Provincial public health authorities were asked to make immediate plans to ensure that test sites were available by mid-October, when it was expected the Red Cross would begin testing donations. They were also asked to take measures to protect the confidentiality of the test results so that no person who wanted to be tested would be discouraged from attending because of a fear that his or her HIV status or sexual behaviour would become known.

The provincial representatives agreed at that meeting that the alternative test sites would be publicized, information would be given to physicians, and counselling would be made available to persons who took the test.

On 19 July 1985, Dr Clayton wrote to the directors of the provincial public health laboratories to confirm that the projected date of Red Cross testing was late summer or early autumn and that every province should establish a testing site by the date the Red Cross began to test blood donations for HIV antibody. He included a summary of the agreements and recommendations made by the provinces at the 4 July meeting and said that information about testing would be available from the National Advisory Committee on AIDS in approximately eight weeks.

Provincial public health officials had not been involved in the early decisions about the implementation of HIV-antibody testing to screen blood donations or the need for alternative sites, even though they would eventually have to establish and operate the alternative test sites. The initial discussions had been between the Red Cross and the National Advisory Committee on AIDS, which had no representation from provincial public health authorities. The provincial representatives on the Canadian Blood Committee had little expertise in public health matters, and in any event they were not involved in discussions about the introduction of testing until 4 June. Then their concern was primarily financial.

The lack of consultation and communication continued through the summer. In September, Dr Gregory Hammond, the director of the provincial laboratory in Manitoba and the chair of the provincial advisory committee on AIDS, wrote to the Laboratory Centre for Disease Control that he perceived

a serious problem of lack of communication and co-ordinated planning between health agencies and various levels of government in Canada, irrespective of the complexities of the situation ... improved interaction between public health officials, laboratory staff and the Red Cross is mandatory, so that we in the provinces, soon to be on the front lines of diagnostic and confirmatory testing and public health follow up, have clear policy directions to plan and carry out our job well. I recommend that each province have a named individual(s) or group which can be contacted for co-ordination with other health care agencies and governments. Regular (verbal) communications would also be useful and should be facilitated ... to update progress and problems.

On 21 October, information about HIV-antibody testing, prepared for health care practitioners by the National Advisory Committee on AIDS, was sent to all provincial epidemiologists. It listed ten groups of persons who were at risk of HIV infection and might require testing. They were:

1. anyone who demonstrates signs or symptoms possibly related to infection;
2. males who have had sex with more than one male since 1979;
3. males whose male sexual partner has had sex with more than one male since 1979;
4. past or present abusers of intravenous drugs;
5. hemophiliacs, especially those receiving Factor VIII prior to July 1, 1985;
6. sexual partners (male and female) of persons in these groups or of persons with a verified reactive HTLV-III [HIV] antibody test;
7. recipients of blood transfusions between 1977 and the commencement of screening of blood donations who develop signs and/or symptoms suggestive of HTLV-III infection;
8. health care workers who have sustained parenteral exposure to blood/body fluids of HTLV-III-infected individuals;
9. persons from areas where HTLV-III infection or AIDS is endemic (e.g. equatorial Africa, Haiti); and
10. recent offspring of any parent belonging to these high-risk groups.

In this material, the National Advisory Committee on AIDS emphasized that the test should be ordered only if it was an appropriate procedure clinically, and if the person understood fully the implications of the test and test results

or the physician believed that the person might otherwise donate blood to obtain his or her HIV-antibody status.

The committee recommended that every province develop a requisition form for HIV-antibody testing. To preserve the confidentiality of results, it suggested that the person be identified on the form by a code recognizable only by the person and his or her physician. Physicians were to be asked to include on the form information about the person being tested. A sample requisition form, sent to the provinces, included the person's date of birth and membership in any of the following risk groups: homosexual or bisexual men, intravenous drug abusers, hemophiliacs, recipients of blood and blood products, persons exposed to HIV parenterally (such as by injection or needlestick injury), immigrants from an endemic area, and sexual partners or offspring of persons who had AIDS or AIDS-related symptoms or who were HIV-antibody positive. The form contained a category, "none," allowing the physician to complete it without designating any risk group. The significance of the "none" category was that it allowed for the testing of persons who might be reluctant to disclose to their physician whether they were members of a risk group. Clinical symptoms, if any, were to be checked off; the categories listed were fatigue, fever, night sweats, diarrhea, weight loss, skin rash, generalized lymphadenopathy (swollen lymph glands), a confirmed case of AIDS, and, again, "none."

The information also contained guidance for physicians about counselling before and after the test. Persons who received positive test results were to be advised not to donate blood, not to share needles, to use condoms during sexual relations, to inform their sexual partners of their positive test results, and not to become pregnant.

The provincial laboratories were accustomed to testing samples provided by physicians for the presence of transmissible infections such as syphilis, gonorrhea, tuberculosis, and hepatitis. For those diseases, they insisted that the person's name be recorded on the requisition form for testing. The emphasis on confidentiality was new. It meant that public health authorities could not identify persons infected with HIV and thus could not advise them about ways to minimize the risk of infecting others and, if necessary, trace their contacts and offer testing and counselling. That task was left entirely to the attending physicians, whose efforts in this respect were difficult to monitor.

In all but three provinces, alternative testing was available by the time the Red Cross fully implemented testing for HIV antibody at the beginning of November 1985, and in some provinces it was available earlier. Manitoba and Alberta were not ready to test samples for HIV antibody until December. Quebec's testing program was not in full operation until March 1986, when the radio-immune precipitation assay (RIPA), the confirmatory test chosen by the Government of Quebec, was perfected. That test, developed by Dr Luc Montagnier in France, was more difficult to carry out than the western blot

test but was believed to be more accurate. Most provinces designated their provincial public health laboratory or laboratories as test sites, but Nova Scotia's public health laboratory carried out testing for all four Atlantic provinces, and Quebec adopted a decentralized approach, designating seven hospitals to perform ELISA testing and its public health laboratory for confirmatory testing. All provinces other than Quebec used the western blot test as a confirmatory test. Although it performed ELISA testing in its public health laboratory, Saskatchewan depended upon the Laboratory Centre for Disease Control for confirmatory testing until June 1986. Some delays in the reporting of test results were experienced by the Atlantic provinces because all the testing was performed in the public health laboratory in Halifax. Newfoundland began conducting ELISA testing in its own laboratory in 1987, as did New Brunswick in the next year, in both cases because of increased demand for testing. In all provinces, the tests were available at no direct cost to the person.

The success of provincial testing in deterring persons from donating blood in order to learn whether they were HIV positive depended in part upon public awareness that the testing was available. In particular, the program had to be explained clearly to members of high-risk groups and the physicians treating them. The amount, timing, and type of publicity with respect to the availability of testing varied. Many of the provinces issued press releases or made other public announcements about the availability of testing shortly before or soon after their facilities were in operation, but the information was not always widely publicized. In Newfoundland, for example, physicians were told of the availability of the new service, but there were no press releases or public announcements. The alternative test sites were not well publicized in Alberta. In Quebec, public health authorities did not begin a major information campaign about AIDS until August 1987; in the two previous years the province had had the highest rate of HIV-infected blood donors in Canada.

In many but not all provinces, information about testing for HIV antibody was distributed to physicians before or soon after the testing was available. Some of the provinces used, or adapted, educational materials prepared by the National Advisory Committee on AIDS. In Newfoundland, because the government had not sent information to physicians, the provincial advisory committee on AIDS decided in May 1986 to send them the information prepared by the National Advisory Committee on AIDS; the government's information was not prepared until 1987. In Nova Scotia, the provincial epidemiologist alerted all physicians to the future availability of testing a month before it began, but the government did not issue its first comprehensive educational materials for physicians until November 1987; in the interval, the Medical Society of Nova Scotia issued its own guidelines, which had been developed with the collaboration of the provincial epidemiologist.

The educational materials for physicians prepared by provincial governments listed groups considered at high risk of being infected with HIV and therefore eligible for testing. Among them, in most provinces, were homosexual and bisexual men and their sexual partners, but the criteria for eligibility for testing varied. Few provinces explained that one of the principal purposes of the testing program was to protect the national blood supply.

In some provinces, such as Ontario, physicians were asked to order a test only if it was clinically indicated. The information sent to physicians in Alberta recommended against routine screening of homosexual or bisexual men who had developed no symptoms of AIDS, and in Nova Scotia physicians were asked to limit testing to "those patients who have a high probability of being infected based upon a careful inquiry into their past medical history and lifestyle." Physicians in some provinces, including Alberta and New Brunswick, were told to order the test only if it was clinically indicated or if the person might otherwise donate blood to learn his or her HIV-antibody status.

Many of the provincial health ministries or health departments devised their own requisition forms for ordering HIV-antibody tests, often adapting the one prepared by the National Advisory Committee on AIDS. In accordance with the committee's suggestions, physicians in some provinces were required to complete the forms in full in order for the tests to be performed. Many of the forms included lists of high-risk groups and of the symptoms of AIDS and AIDS-related diseases, and the physician was expected to check off those that applied to the person. On other forms, physicians were asked to write in the risk group of the person being tested. In several provinces the lists of high-risk groups and of symptoms contained a final category of "none" or "other," permitting persons to be eligible for testing who might have been reluctant to disclose their membership in a high-risk group to a physician.

Most provinces followed the recommendations of the National Advisory Committee on AIDS with respect to the confidentiality of test results. Most asked physicians to identify the persons on the requisition form by a code that would permit the physician, but no one else, to link the test results to the person.

The information sent to physicians also contained advice about counselling persons before and after testing, with the provinces reproducing or adapting the recommendations of the National Advisory Committee on AIDS.

The consequences of delay in testing

The delay in implementing HIV-antibody testing had tragic consequences. I accept the estimate of Dr Robert S. Remis, an epidemiologist, formerly the director of the regional bureau of infectious diseases in Montreal and now

a consulting epidemiologist with the AIDS bureau of the Ontario Ministry of Health and an associate professor in the department of health sciences of the Faculty of Medicine at the University of Toronto, that in 1985 approximately 380 persons in Canada were infected with HIV by blood transfusion. Approximately 193 of those would have survived "early mortality" – that is, they would have survived the first three years after transfusion. (Most of the others would have died from causes related to the condition for which the transfusion was administered.) Of these 193, approximately 133 (just over two-thirds) were infected after the beginning of March 1985, when test kits were approved in the United States and became commercially available. Table 12.1 illustrates, on a cumulative basis, the number of HIV-infected transfusion cases Dr Remis estimates could have been prevented had HIV testing been started earlier than November 1985. If testing had been implemented in Canada in March, as soon as test kits became commercially available, approximately 133 cases of HIV transmission could have been prevented. If testing had been implemented in Canada in May, after testing had been implemented in Australia and virtually all of the United States, approximately 97 cases could have been prevented.

These figures are conservative. They exclude all who would have died within three years even if the cause of death ultimately was AIDS. They also exclude cases of secondary transmission caused by those infected by transfusion (including those who did not survive early mortality) transmitting the disease to other persons.

Table 12.1
HIV transfusion: Preventable cases in Canada, March–October 1985

Month	Preventable cases (cumulative)
October	12.8
September	25.8
August	43.7
July	61.6
June	79.5
May	97.4
April	115.3
March	133.2

Source: Dr Robert S. Remis, director of regional bureau of infectious diseases, Montreal (1995)

Commentary

At the heart of the delay in introducing HIV testing was the character of the Red Cross, the organization most responsible for ensuring the safety of the blood supply. The Red Cross was a tentative and ineffective decision maker that recoiled from its responsibility to make timely decisions on matters of safety. Because of the relationship of distrust and misunderstanding that had developed with its funder, the Canadian Blood Committee, it was reluctant to take measures that would cost the provinces money without first obtaining an outside stamp of approval. Because of its fear of public controversy and the need to protect all Red Cross programs from negative public opinion, it was reluctant to make decisions that raised a risk of unfavourable publicity. It preferred to delegate those decisions to an outside body. As a result, it delegated its responsibility for decision making on the issue of testing to the National Advisory Committee on AIDS. For its part the Canadian Blood Committee, once presented with an implementation plan to approve, reacted with routine deliberation at a time when expeditious action was required. Once approval had finally been granted, Canada took longer to implement testing than other nations.

In the background, the federal government failed to take any significant role in urging the implementation of HIV-antibody testing or otherwise regulating the collection of whole blood and the distribution of blood and components.

At that time, blood and blood components were not regulated by the federal government. By contrast, blood products, which were manufactured from plasma, the liquid part of whole blood, were regulated by the Bureau of Biologics, which could regulate the manner of collecting the plasma that went into the products. The federal government could, and did, require that such plasma be tested for hepatitis B and syphilis. The federal government could also have required that the plasma be tested for HIV antibody when such a test became available. Since the majority of the plasma that went into Canadian blood products was taken from the same whole-blood donations, a regulation that required HIV-antibody testing of plasma would have effectively required testing of whole-blood donations, and would have reduced the risk of HIV in the red blood cells and platelets that were obtained from the donations.

The process of implementing HIV-antibody testing was characterized by a failure of all the major actors responsible for the provision of blood services to heed the clear indications of urgency and to react quickly and appropriately. The delay can be examined in three phases: the consultation with the National Advisory Committee on AIDS, the approval of funding by the Canadian Blood Committee, and the implementation itself. Each phase contributed substantially to the delay.

Phase 1: Consultation with the National Advisory Committee on AIDS

Consultation with the National Advisory Committee on AIDS began in October 1984, when testing for HIV was on the horizon, and ended seven months later, in May 1985. By this time, testing had been licensed and was near full implementation in the United States. Australia had also implemented testing.

In 1985, there was no regulator supervising whole-blood collections and no legal requirement that the Red Cross consult anyone before instituting a new test for whole blood. The Red Cross was the body responsible for delivering safe blood and components to hospitals and patients. As such, it had previously instituted tests for hepatitis and syphilis without consulting any federal body. Testing blood donations for HIV antibody was just as much a part of the Red Cross's obligation to ensure the safety of blood. As early as August 1984, when the initial approach to the National Advisory Committee on AIDS was made, the Red Cross knew that once HIV-antibody test kits became licensed and available, it would have to implement the test and remove from the blood supply those donations that tested positive.

It was inappropriate for the Red Cross to delegate the decision on testing to the National Advisory Committee on AIDS. That committee had no power to do anything but advise. It could not authorize funding of any new test. Moreover, the committee was ill-suited to reach a decision on the implementation of HIV-antibody testing. It did not have adequate resources to deal with the matter on an urgent basis. It met only twice a year – at a time when developments in AIDS research were occurring very quickly. It is true that HIV-antibody testing brought with it complications not present in other tests. AIDS was a new disease, a fatal disease, one that carried a most terrible stigma. The Red Cross was legitimately concerned that persons at risk of contracting AIDS might donate blood as a means of finding out whether they were infected and that some of those donations could pass undetected through the screen and go on to infect other persons. Equally, it was prudent of the Red Cross to consult with the National Advisory Committee on AIDS on other issues, such as the provision of alternative test sites, the confidentiality of test results, and the notification of infected donors.

There is a difference, however, between consulting outside experts and abdicating responsibility to another body. It is clear from the record that the Red Cross did not approach the National Advisory Committee on AIDS with its implementation plan for advice as much as for approval. The relationship between the Canadian Blood Committee and the Red Cross had deteriorated to the point that the Red Cross would not even provide that committee with a funding estimate before securing formal approval for HIV-antibody testing from the National Advisory Committee on AIDS. In that way, it would be the decision of the National Advisory Committee on AIDS – rather than a proposal from the Red Cross – that was brought before the Canadian Blood Committee. It is not productive at this stage to analyse who was more responsible, the

Red Cross or the Canadian Blood Committee, for the disintegration of their relationship. The climate of distrust ensured that the cooperation necessary for quick action would be impossible.

The members of the National Advisory Committee on AIDS and its secretariat should have been conscious of its limited role and resources. While it was appropriate that the National Advisory Committee on AIDS provide what advice it could, it should not have passed a motion making the introduction of testing blood contingent on the report of its task force. Once having accepted that responsibility, however, it was incumbent on it to act quickly. It did not do so.

Why the task force took so long to be organized is not clear. By January 1985, three months after the meeting that recommended its establishment, few steps had been taken. What is clear, however, is that the potential value of a task force study was much less apparent by January 1985 than was the need for quick action. The Laboratory Centre for Disease Control, as the secretariat for the National Advisory Committee on AIDS, decided to proceed with the task force at that time for no better reason than that it had been called for by the committee.

At the very least, the task force should have met within a very few weeks. Instead it did not meet until March, and the National Advisory Committee on AIDS did not consider its recommendations until mid-May. During this period, the Red Cross did not press forward with implementation or seek funding from the Canadian Blood Committee. Concurrently, senior officials of the provincial departments of health that would be called upon to create alternative test sites were not brought into early discussions about them.

Thus, for more than nine months, the implementation of testing was delayed. The involvement of the National Advisory Committee on AIDS took up much precious time and added very little value.

Phase 2: Funding by the Canadian Blood Committee

The Canadian Blood Committee did not approve funding for HIV-antibody testing until 1 August 1985, eight weeks after the Red Cross had presented its budget request. It must be noted, however, that the Red Cross implementation plan proposed approval only by 30 June. Although all provinces were responsible for the delay in funding up to 12 July 1985, the final three weeks of delay resulted from the inaction of the Ontario government.

The Canadian Blood Committee was not well-suited for making decisions on urgent matters. It was limited in autonomy and in its ability to make quick decisions. On major funding issues, each member normally had to seek approval from his or her government. The Canadian Blood Committee was, however, capable of acting with dispatch when it recognized a situation as urgent. An instance, reviewed in Chapter 15, occurred in January 1985, after the Bureau of Biologics ordered the use of heat-treated factor concentrate only. Because Connaught Laboratories Limited (Connaught) was unable

to produce a heat-treated product for some months, the Red Cross necessarily had to buy factor concentrate elsewhere and cancel orders to Connaught for non-heat-treated concentrate. At a meeting of the Canadian Blood Committee on 15 and 16 January 1985, Connaught asked for a temporary relief package to compensate it for the money it would not receive from sales to the Red Cross. A relief package was negotiated by the Red Cross and two members of the Canadian Blood Committee's executive committee and approved in principle by the executive committee at its next meeting on 17 April. It provided for monthly payments to be paid to Connaught of up to \$150,000 per month, subject to adjustments, for up to six months. Between this meeting and the full meeting of the Canadian Blood Committee on 4 and 5 June 1985, two payments of \$150,000 were made. Upon further analysis by the Canadian Blood Committee's secretariat, the payments were adjusted to reflect the poor yield of factor concentrate that Connaught had historically produced. This money came not from the Canadian Blood Committee, but from a fund held in trust by the Red Cross for the provinces in its "fractionation account." Stephen Dreezer, a member of the Canadian Blood Committee, testified that the relief package was delivered in this manner because there was an understanding of "good faith" and because there was "a lot of urgency to the situation." One can conclude either that members of the Canadian Blood Committee did not appreciate an equal urgency in the need for HIV-antibody testing, or, contrary to the advice of the Red Cross and the National Advisory Committee on AIDS on 4 and 5 June 1985, chose to delay the implementation of testing until after alternative test sites were in place.

Some governments, particularly Ontario, became preoccupied with time-consuming formal budget approval rather than quick action. Further, contrary to the recommendation of both the Red Cross and the National Advisory Committee on AIDS, the Canadian Blood Committee delayed its approval for funding until after the issue of alternative test sites had been resolved at the 4 July federal-provincial meeting.

It is equally difficult to understand why members of the Canadian Blood Committee were not given the information required to authorize funding until they met on 4 and 5 June. As early as the 7 March 1985 meeting of the task force, it was already apparent that the committee would be called upon to fund HIV-antibody tests and what the approximate cost would be. It was similarly apparent that there was a need for quick action. Dr Leclerc-Chevalier was at this meeting and the 15 May meeting of the National Advisory Committee on AIDS, yet she did not prepare the individual members of the Canadian Blood Committee to be in a position to approve funding at their next meeting. Nor did the Canadian Blood Committee secretariat attempt to analyse the Red Cross's supplementary budget before that meeting.

The Red Cross, for its part, had estimated the costs of HIV-antibody testing before the National Advisory Committee on AIDS met in May, but chose not to forward the estimate to the Canadian Blood Committee until the National

Advisory Committee on AIDS had approved the implementation plan. It did not wish to second guess the National Advisory Committee on AIDS. As a result, the Canadian Blood Committee did not receive a budget request until the late date of 21 May. Mr Hearn, the chair of the Canadian Blood Committee at the time, commented on this delay in his testimony:

The Red Cross, in August – at least August of 1984, was very clearly of the view that AIDS testing was going to come forward ... you don't need to go into the records to establish that because they told the CBC [Canadian Blood Committee] that they thought that was going to come.

We wait then for months and months and months, and then the Red Cross comes to the CBC with a document on May 21st of the following year in which they now say it is not even – they don't even say it is a matter of the highest urgency in their submission – they say that we are making a submission that will require you to fund for AIDS testing.

Now, the Red Cross understood the nature of the CBC. We had now, by this time, almost four years of developing a relationship, the Red Cross understood that we had to check with our governments. The Red Cross understood the nature of the process. The Red Cross understood that the CBC could not make an instant decision. They knew that. They knew that before they ever came to it and they would acknowledge that. I think the Red Cross would always acknowledge that. So I raise, in my own sense, the question, "Why are we being provided with a document on May 21st, that requires an instant answer," when the organization that had the expertise, that had the knowledge, that had the most involvement in the blood system of any in the country, knew this was coming? Knew that it had to go into place, knew that it was going to be urgent? Why were they coming on May 21st with a document that said, "We are going to require so many weeks of planning here"? Why were they not coming with a document that said, "We are ready to go today, gentlemen. Today we are ready to go. We need your approval today." They didn't say that. They said, "We want you to give us a direction as quickly as possible."

Indeed, if anyone was familiar with the cumbersome nature of the Canadian Blood Committee's budget approval process, it was the Red Cross. It was, at best, unrealistic to believe that the provincial governments could all reach approval between 5 and 30 June.

Although the funding approval by the Canadian Blood Committee was unacceptably slow, this did not relieve the Red Cross from the responsibility of acting on its own to protect the nation's blood supply by continuing to prepare for the implementation of testing. Its most evident failure was its cancellation of the training session scheduled for 29 and 30 July. By mid-July, it was obvious to all concerned that HIV-antibody testing of blood donations would have to take place soon. It was also obvious that the persons who

would do the testing would have to be trained. The relatively modest funding required to conduct the training would have been well within the immediate means of the Red Cross. Yet, despite these facts, the Red Cross did not commit any of its own resources to allow this necessary step to go forward.

The training seminar is merely an example. The Red Cross had sufficient resources, including cash on hand, to bring HIV-antibody testing to the verge of implementation before formal approval was granted by the Canadian Blood Committee. The Red Cross argued that it was prevented by the Canadian Blood Committee from spending any money without the committee's approval. That may be the reason why the Red Cross did not fully implement testing without the committee's approval. If, however, as its senior officials testified, it was aware of the public health emergency of HIV in the blood supply, there was not a sufficient justification for an organization with the means of the Red Cross to refuse to take such a modest and necessary step towards implementation as training its staff. As an organization aware of the urgency of the situation and its responsibility to maintain the safety of the blood supply, it should have taken these steps following the approval in principle by the Canadian Blood Committee without waiting for formal approval.

Phase 3: Implementation Period

The time required for implementation was unreasonably long. The Red Cross told the National Advisory Committee on AIDS and the Canadian Blood Committee that testing would be implemented in eight to ten weeks following the approval of funding. By the time of the federal-provincial meeting on 4 July 1985, that estimate had increased to ten to twelve weeks. No explanation for the increase was offered. Ultimately, the time from the approval of the funding to full implementation was more than twelve weeks, although partial implementation occurred starting in late September, approximately eight weeks after the approval. In the United States, implementation occurred very rapidly in high-risk areas, and full implementation was achieved in most of the country by April and May. In Australia, testing was begun in April and completed in May. What the Red Cross proposed and went on to effect was a methodical and time-consuming process, reflecting a failure to appreciate the urgency of the situation. The plan had been approved by both the National Advisory Committee on AIDS and the Canadian Blood Committee, however, with neither organization offering criticism of the schedule.

Dr Davey testified that the requirement for pre-market evaluation of the test kits was one of the factors that delayed the implementation of testing. He said he was surprised by "the whole business" of the evaluation by the Bureau of Medical Devices, about which the Red Cross had not been consulted. If it had not occurred, he said, the Red Cross would have proceeded differently. It had been prepared to start implementation in high-risk areas first, and then to proceed with full implementation at a later date. The record does not support the suggestion that the approval by the Bureau of Medical

Devices delayed the Red Cross. Evaluation of the kits took place in the spring of 1985. At the meeting of the National Advisory Committee on AIDS of 15 May, it was announced that approval would come shortly. On 28 May, a week before the Red Cross plan was put before the Canadian Blood Committee, the first manufacturers of test kits were told that there was no objection to the distribution of their kits in Canada for screening purposes. This was four months before the implementation by the Red Cross began. The Red Cross was officially informed of the bureau's approval on 11 June 1985, well in advance of funding approval by the Canadian Blood Committee. The Red Cross, however, was unwilling to make any financial commitment before it had received approval from the Canadian Blood Committee. In these circumstances, the date of approval by the Bureau of Medical Devices was immaterial. Dr Gill, the director of the Bureau of Microbiology at the Laboratory Centre for Disease Control, which actually conducted the evaluation, testified that the Red Cross had not at the time indicated that pre-market evaluation presented an obstacle to implementation. Had it done so, he said, the evaluation would have been expedited.

Provincial testing for HIV antibody

Several provinces did not fulfil the commitments made at the July 1985 federal-provincial meeting at which it was decided to establish alternative test sites. A primary reason for establishing provincial test sites before or by the time the Red Cross introduced testing to screen blood donations was to deter persons at high risk of infection with HIV from donating blood to the Red Cross in order to learn their HIV status. To the extent that the commitments were not fulfilled, there was an increased risk that those persons might attend blood donor clinics for that purpose. If they did so during the "window period" of infection, when the antibody could not be detected, they might thereby contribute to the contamination of the blood supply.

The provincial representatives had also agreed on the importance of confidentiality in test results. That decision was important because some persons at high risk might be reluctant to undergo testing through a provincial laboratory if the government could learn their identity. The majority of provinces decided to test by code. Under this system, only the physician and the person being tested were supposed to be able to link the laboratory results with the person in question. Anonymous testing, in which there was no way for anyone except the person being tested to know the result, was used by only one clinic in Ontario.

For the most part, the test sites were not adequately publicized, although public awareness of their existence, particularly among members of high-risk groups, was essential to their success in deterring persons from donating blood to learn their HIV-antibody status. In February 1985, the U.S. Food and Drug Administration recommended to blood collection agencies in that

country that they alert every prospective donor to the existence of alternative test sites. No similar recommendation was made in Canada, nor was the existence of alternative test sites publicized at the Red Cross blood donor clinics.

Educational materials for physicians were intended to alert them to the availability of the provincial test sites, to give information about the test, and to assist in providing counselling to persons before and after the test. These materials were not ready in some provinces before the introduction of testing and did not always explain the importance of the provincial sites in deterring persons at high risk from donating blood to the Red Cross.

An important principle underlying the establishment of the provincial test sites was that testing was to be universally available and was to be performed at no cost to the person tested. All persons who perceived themselves at risk of infection with AIDS were to be eligible. Although the test was provided by the provinces at no charge, the criteria for eligibility suggested in some provinces appeared to restrict testing to persons who fell within the prescribed categories. In some provinces, homosexual or bisexual men were eligible only if they had had more than one sexual partner. Furthermore, in some provinces tests were only to be ordered if "clinically indicated." This would probably exclude persons who did not admit that they belonged to any group at high risk for AIDS, and did not possess any symptoms of AIDS.

Before this Inquiry began, in testimony before the subcommittee on Health Issues of the House of Commons Standing Committee on Health and Welfare, Social Affairs, Seniors and the Status of Women, the Red Cross suggested that a cause for the delay might have been a shortage of test kits on the international market until the fall of 1985. No evidence of such a shortage appeared at the Inquiry. Indeed, the implementation of testing in Australia in April and May 1985 demonstrates that there is no basis for the contention that a shortage existed.

13

Notifying the Recipients of Contaminated Blood and Blood Components

After the Canadian Red Cross Society (Red Cross) began to test all Canadian blood donations for HIV antibody in November 1985, the vast majority of HIV-infected donations were screened out of the blood supply. The only exceptions were donations, few in number, missed by the HIV-antibody test, usually because, at the time of donation, the donors were in the window period of infection, during which time the virus could not be detected. There remained, however, a substantial number of persons who had received blood components before testing began and who may have been infected with HIV. Because of the long latency period between infection and the development of AIDS or AIDS-related symptoms, it was likely that there were many recipients of transfusions, infected and infectious, who were unaware of their condition. The precise number was, of course, unknown.

What follows is a consideration of the methods, and the success of those methods, by which recipients of infected or potentially infected blood components were notified of the possibility of their infection. Notification was important for three reasons. First, persons who were infected and unaware of their infection could infect others. Second, it was important that those infected with HIV be made aware of their status so that they could take advantage of the treatments that became available and continued to become available. Third, persons who had been infected had a right to know what had happened to them.

There were several methods by which persons could be notified of the risk of infection from blood components. When a donor was identified as infectious, his or her previous donations could be traced, if records were available, and the recipients of those donations could be notified. This type of notification became known as "look-back." Another method was for hospitals to identify, from their records, former patients who had received blood components and inform them directly of the risk of HIV transmission from transfusion. This is often referred to as "targeted notification." A third method was to carry out a public education campaign, advising persons who had

received blood components between 1977 (the emergence of AIDS) and November 1985 (the full implementation of testing) to consider having an HIV-antibody test. All three methods of notification were used at various times.

The success of recipient notification was, at best, limited. In every region of the country, infected persons testified that they had been given no notice that they had received, or might have received, infected or potentially infected blood components. They had learned of their infection only years later, when they began to experience symptoms or had been tested for HIV for some other reason, such as an application for insurance.

The information required in order to notify recipients was spread among several sources. The Red Cross had information about donors who had tested positive to HIV-antibody tests. It had records of any prior donations from those persons and the names of the hospitals that had received the blood components from those donations. In provinces in which the reporting of AIDS was nominal, that is, in which cases of AIDS had to be reported to the government with the name of the person infected, public health officials possessed the names of persons diagnosed with AIDS who might have been blood donors. Hospitals, in theory at least, possessed records identifying patients who had received blood components. Physicians possessed information from which patients could be located. If all these organizations or persons had kept sufficient records and had communicated with one another, it should have been possible to trace a large number of the recipients of contaminated blood transfusions. In practice, it was much more difficult.

Recipient notification before the implementation of HIV-antibody tests

Two terms commonly used in discussions of recipient notification are "trace-back" and "look-back." These terms are not always used with precision. A trace-back is the process followed in identifying the donor of an infected blood unit after a person who has received a blood component develops AIDS or is found to be HIV positive. In other words, there is a trace-back from the infected recipient to the infected donor. A look-back is the process followed to identify the recipients of blood components from a donor who has proved to be infected. A donor may be identified as infected as a result of a trace-back from an infected recipient or during the test of a blood donation for HIV antibody. Donors may also be identified as infected through other means, including a physician's diagnosis, and the appropriate Red Cross blood centre may be informed as a result. Once the donor is identified as infected, all his or her previous donations are traced and the recipients notified.

Trace-backs did not originate with the emergence of AIDS. They had been used on occasion by the Red Cross in connection with another blood-borne pathogen, hepatitis B. If the medical director of a blood centre received a report of hepatitis B in a recipient of blood or blood components, a trace-back was

undertaken to determine whether any donor of the blood components received by that person was infected. A trace-back might not be undertaken if the recipient had received components from a large number of donors. The purpose of the trace-backs was to identify and find the donor, who might be a carrier of the disease even if he or she was not suffering from any symptoms. There was, however, no policy of look-backs to identify and inform recipients of infected blood or blood components. The latency period of hepatitis B, which is approximately one to three months, is much shorter than that of AIDS; it was therefore unlikely that many persons who were infected through a transfusion could be reached by look-backs before the symptoms appeared.

By the autumn of 1984, when data were being released from preliminary HIV-antibody tests conducted at the National Institutes of Health in the United States and the Laboratory Centre for Disease Control in Canada, it was believed that the latency period between infection with HIV and the development of AIDS was between two and five years. Thus, an infected blood donor might remain symptom-free and continue to donate blood, if not screened out, for several years. The potential ramifications of this were serious. For example, if a reasonably regular blood donor were to donate ten times in a four-year period after he or she became infected but was still symptom-free, and each donation was separated into three components – red cells, platelets, and plasma – and each component was transfused into a different recipient, thirty persons could be infected. A look-back following the identification of one infected donor might therefore involve a very large number of recipients. If the plasma component of that donation were pooled in order to make fractionated blood products, many more persons could be exposed to the virus. The recipients of those components or products would likely be unaware of their condition, and they or their potentially infected sexual partners might also give blood.

The first difficulty in identifying recipients of infected components was in identifying donors who were infected. Until late in 1985, there was, in Canada, no widely implemented test that could detect HIV antibody and, by that means, identify donors who were HIV-antibody positive. Infected donors would not be diagnosed until they had developed the symptoms of AIDS, and then the only sources of information about them were the physicians caring for them, public health officials, and the persons with AIDS themselves.

On 10 December 1984, a joint statement was released by the principal organizations of blood bankers in the United States – the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers – regarding the identification of blood donors who developed AIDS and the disclosure of information to the recipients of blood components or blood products derived from their donations. The first recommendation said:

Physicians in blood collecting organizations and transfusion services should urge public health investigators and physicians to ask all patients with AIDS if they have donated blood or plasma within the past five years.

If such donations did occur, physicians in charge of the blood collecting organization should be informed of the donor's name and the date(s) and location(s) of donation(s).

The joint statement added that, once a potentially infected recipient had been identified,

information should be transmitted to the medical staff of the hospital transfusion service. At that time a decision should be made as to who will inform the recipient's physician. The decision to tell patients (or family members) that they have been transfused with products donated by individuals who later developed AIDS should be made by the patients' physicians. In most cases we believe it proper for the patient, or in special circumstances a guardian or responsible family member, to be informed.

There was no similar recommendation or policy in Canada. The decision to undertake measures to identify infected donors or recipients was within the discretion of the local medical directors of Red Cross blood centres. In most cases, the measures taken focused on the donors. For example, in July 1983, Dr Raymond Guévin, the medical director of the Montreal blood centre, conducted a trace-back upon receiving a report that an infant had contracted AIDS after a transfusion. Five donors were involved. Dr Guévin communicated with all five, one of whom he believed to be homosexual. After a few telephone calls, the Red Cross lost contact with that man, but concluded that this was the first time he had donated blood in Quebec. There was not, however, any national donor registry from which it could be determined if he had donated elsewhere in Canada. Nor was information about him conveyed to the other sixteen blood centres to enable them to review their own records. The Red Cross had no policy that encouraged a systematic exchange of such information among blood centres.

In another example, in British Columbia in the summer of 1985, the Red Cross blood centre undertook trace-backs after two recipients of transfusions developed AIDS. By this time, HIV-antibody testing was available from the Laboratory Centre for Disease Control in Ottawa, although testing had not yet been implemented by the Red Cross or the provincial public health laboratories. The two patients, one of whom had been severely burned, had received components from 366 donors. The trace-back involved communicating with all these donors to ask that they be tested for HIV antibody, there being no bank of samples from their donations that could be tested. Three hundred and four donors agreed to be tested. One was found to be HIV-antibody positive. A second donor had died of a clinical condition that may have been AIDS. The process of tracing was extremely time-consuming, requiring, on average, between one and two hours per donor, since many of the donors had moved since their last donation.

Shortly before the introduction of HIV-antibody testing, a pediatric patient in Nova Scotia who had received multiple transfusions died of AIDS. Trace-backs revealed one infected donor who had given blood three times previously. Look-backs of other recipients of components from that donor revealed eight persons, still living, who were HIV-antibody positive.

Sharing of information between public health agencies and blood centres

In the United States, before the introduction of HIV-antibody screening in the spring of 1985, some blood banks were doing more than simply tracing infected recipients. The Irwin Memorial Blood Bank in San Francisco received from the San Francisco health department the names of persons diagnosed with AIDS. Irwin Memorial checked the names against its donor register and then traced the recipients of blood components from any infected donors. Similarly, as early as August 1983, the public health service in Orange County, California, compiled a list of persons who had died of AIDS and gave the list to the American Red Cross, which checked it against its donor list.

A study by California blood bankers, California public health officials, and the U.S. Centers for Disease Control in 1989 examined the effectiveness of various methods used between 1981 and 1989 for tracing donors and recipients of HIV-infected blood components. It found that the comparison of public health lists and donor lists, first employed at Irwin Memorial, was by far the most effective means of identifying infected donors or recipients.

In Canada, local public health officials and the Red Cross only infrequently exchanged information about persons infected with AIDS. In most provinces, there were legal barriers to giving information of this kind to the Red Cross. No legislation was enacted in Canada to allow public health authorities to give the names of persons infected with AIDS or HIV to the Red Cross, nor, with the exception of Nova Scotia, which is discussed later in this chapter, was there any legislation to require the Red Cross to disclose the names of its donors to public health authorities. In Newfoundland, Quebec, and Manitoba, AIDS was not made a reportable disease until after 1986.

The Canadian Red Cross discussed the usefulness of obtaining information about infected donors before testing was implemented. In September 1983, the AIDS working group learned of a suggestion of the Red Cross's apheresis-component working group that blood centres be informed about persons with AIDS in order to determine whether they had donated blood; if they had donated, recipients of components from their donations could be traced. The AIDS working group consisted of senior persons from the national office of the blood transfusion service, several local medical directors, and representatives of the blood donor recruitment, public relations, and nursing

departments of the Red Cross. On 23 November 1983, the subject arose at a meeting of another Red Cross body, the immunology-virology working group. The minutes record that:

The group discussed the concerns of some Centre Medical Directors on the identification of AIDS patients who may have been former blood donors. There is no mechanism for communicating such identification between the CRC BTS [Canadian Red Cross blood transfusion service] and provincial or federal health authorities at present. However, the group agreed that such communications are necessary in order to identify potentially infective units of blood and blood components.

Drs Davey and Derrick indicated that a list of provincial public health officials, from whom the NBTS [national blood transfusion service] could obtain such information, could be obtained from Dr Clayton at the LCDC [Laboratory Centre for Disease Control]. A liaison could then be established between these individuals and Centre Medical Directors to obtain information of this nature. Identification of AIDS patients who may have been previous blood donors would be held in strict confidence by BTS Centres. By establishing such a tracing mechanism, further information may be obtained on whether or not blood is a significant vehicle of transmission of AIDS.

Dr Martin Davey was then the assistant national director and Dr John Derrick was the adviser, regulatory affairs and good manufacturing practices, of the blood transfusion service of the Red Cross. Dr Alastair Clayton was the director of the Laboratory Centre for Disease Control, a part of the Department of National Health and Welfare, Health Protection Branch. The Laboratory Centre for Disease Control was the federal body responsible for epidemiological surveillance, laboratory surveillance, and the diagnostic systems of disease control in Canada.

The national public health authorities at the Laboratory Centre for Disease Control did not have any organized or systematic means of gathering information about infected persons or exchanging such information with the Red Cross. Although a form for reporting cases of AIDS to the Laboratory Centre for Disease Control was distributed, it was not distributed to all physicians and did not ask whether the patient had ever donated blood. By contrast, in 1981, the laboratory centre had sent out an information letter to all physicians in Canada informing them about toxic shock syndrome and including a form for the reporting of any suspected occurrences to the centre. It was only in 1986 that the centre distributed a form for reporting AIDS that included a question asking about blood donations.

On 22 November 1983, Dr Gordon Jessamine, the chief of the Field Epidemiology Division of the Bureau of Epidemiology, Laboratory Centre for Disease Control, wrote to Dr Roger Perrault, the national director of the blood transfusion service of the Red Cross, to inform him of a report he had received about a patient with Kaposi's sarcoma (an indication of AIDS) who had been a blood donor. Dr Davey replied, on 2 December 1983, on behalf of Dr Perrault, as follows:

[T]he Blood Transfusion Service [BTS] has recognized the need to trace the disposition of blood donations when donors subsequently develop AIDS, and to trace recipients of any of the products of these donations. This requires adequate identification of the patient (name, date of birth, residence) and the best available information about when and where blood was given. The BTS Centre concerned can then identify the recipients of all products, and obtain current clinical information about them. Similar tracking of products and recipients is done regularly in relation to hepatitis. It goes without saying that information about the donor with AIDS and the recipients is to be kept confidential, and that the latter will be contacted through their own physicians in a way that should not cause unjustified anxiety.

Notification of cases of AIDS to the relevant BTS Centres by provincial health departments would enable early tracing. To ensure that none fall through the net, details of new cases reported to LCDC could be sent here for notification to centres. The results of centres' investigations can be reported here and collated for you.

The Laboratory Centre for Disease Control did not have the name of the donor to provide to Dr Davey. It might have given him the name of the donor's physician, although there was no record that anyone at the laboratory did so.

Dr Davey's letter suggested a role for provincial health departments in tracing infected recipients. As already noted, privacy legislation prevented the exchange of such information. Provincial health authorities, moreover, did not seek such information for their own purposes.

In Ontario, for example, beginning in 1985, physicians requisitioning an HIV-antibody test were required by regulation to complete a form that asked, along with other information, for the date and place of any donation of blood or blood components. That portion of the form was often not completed. The Ministry of Health took no action to ensure that physicians completed the form properly. Even when the forms were fully completed, however, the ministry had no legal means of informing the Red Cross about the infected person's history of blood donation, if any. Indeed, communicating this information would have been a violation of the public health legislation in Ontario, which prohibited its disclosure.

The importance of completing the form was not fully communicated to physicians. Dr Philip Berger, a Toronto physician who specializes in the treatment of HIV-infected persons, testified that he had never asked his HIV-infected patients whether they had donated blood. He stated:

I had presumed that somehow the Red Cross is going to know about who had tested positive and was going back to old blood to find out if that old blood was tested positive. It was a general sense that I had.

Had I known that there was any dependence on reporting the names of people who had advised me about donating blood, I would have ... asked them if they had donated blood, which I wasn't doing, and I likely would have reported because I would have understood clearly what the implications were.

Provincial governments did not ask physicians to encourage patients who had AIDS or were HIV positive, and who had donated blood, to consent to allowing their conditions to be revealed to the Red Cross so that it could initiate look-backs. In some instances, physicians who treated persons with AIDS did, on their own initiative, ask persons with AIDS whether they had donated blood and then told the Red Cross about those who had donated.

Issues of notification raised by implementation of HIV-antibody testing

On 1 May 1985, the Red Cross completed a plan, prepared in the previous month, for implementing HIV-antibody testing in Canada. Testing was fully implemented in November 1985. At the outset, it was apparent that there were issues of whether and how recipients of potentially contaminated blood components from previous donations by a person who was identified by the new tests as HIV-antibody positive should be notified of this fact.

On 7 June 1985, a joint statement about HIV-antibody tests was released in the United States by the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers. It included the following recommendation with regard to notification of recipients of blood components prepared from previous donations by a person who had been identified by the new tests as HIV-antibody positive:

Studies are underway to evaluate the health status of recipients transfused with components from donations that were subsequently determined to contain HTLV-III [HIV] antibodies. Because we do not know what these studies will show, and because we do not know whether an individual with HTLV-III antibodies at a current donation had such antibodies previously, an adequate basis for notification of recipients of blood components from a previous donation does not exist. The injury to prior recipients which

may be caused by such notification is disproportionate to the benefits which are tenuous and ill-defined. As information about the natural history and relative risk of the antibody state develops, modified recommendations will be forthcoming.

If components from previous donations are still in inventory, they should be recalled, tested and destroyed. When testing (including verification) reveals the presence of HTLV-III antibodies, the physicians responsible for the care of patients who received other components from that donation should be informed by way of the transfusion service director. These physicians, in turn, should decide whether to inform the recipient, or his parent or guardian. These recommendations are made with full knowledge that as additional information develops, any or all may become obsolete. Moreover, although there is no current federal requirement for donor testing or notification, many states have regulations which will affect the donor notification procedure. For blood collection agencies in areas where no regulations regarding donor notification are in effect, decisions should be made in a way that recognizes both the inadequate state of our current knowledge and the potential for harm if inaccurate information is transmitted to donors or recipients.

It must be remembered that at that time the full significance of a positive test was not known. Although it was understood by that time that the presence of HIV antibody was indicative of HIV infection, it was not known what proportion of those persons infected with HIV would develop AIDS.

On 11 July 1985, senior members of the Red Cross blood transfusion service discussed several issues, including HIV-antibody testing, with members of the federal regulatory body, the Bureau of Biologics, which was part of the Department of National Health and Welfare, Health Protection Branch. Dr Derrick, for the Red Cross, suggested that recipients not be notified until such time as they could be treated effectively. Dr John Furesz, the director of the Bureau of Biologics, suggested that the issue "was really one of ethics" and supported Dr Derrick's recommendation about notification.

On 22 July 1985, the U.S. Food and Drug Administration released "recommendations concerning blood or plasma previously collected from donors currently HTLV-III [HIV] antibody positive." It recommended that, when a donor was found to be HIV-antibody positive, there be a look-back to his or her prior donations. The extent of the look-back would depend upon the type of component and the length of its expiry period. With respect to notification of recipients, the Food and Drug Administration stated:

Notification of prior recipients of products from HTLV-III [HIV] antibody positive donors is a complex issue about which there is a great deal of uncertainty at the present time because of our incomplete understanding of the meaning of a positive HTLV-III antibody test result. We believe that

consideration must be given to such a broad range of factors, many of which will be unique to a given situation and/or facility, that decisions in this area should be made at the local level. Also, although it might be ideal to share information with other establishments known to have recently collected blood or plasma from the same donor, we recognize the confidentiality concerns, which may include state or local restrictions, may preclude this in many instances.

On 12 August 1985, Dr Albert Liston, the assistant deputy minister in charge of the Health Protection Branch of the Department of Health and Welfare, sent these recommendations to two other senior officials, Dr Alastair Clayton, the director of the Laboratory Centre for Disease Control, and Dr Denys Cook, the director general of the Drugs Directorate, of which the Bureau of Biologics is a part. Dr Liston made the following comment:

The attached from the US raises the question of the adequacy of Canadian procedures to minimize risk from blood products derived from donations contaminated with blood having an HTLV-III positive titer. Have we addressed the "look-back" provisions as in the US?

Two days later, Dr Furesz, the director of the Bureau of Biologics, wrote to Dr Wark Boucher, the chief of the bureau's Blood Products Division, asking him to prepare a reply for Dr Cook's signature. Dr Furesz asked:

How can we enforce a "look-back" procedure in CRC [the Canadian Red Cross Society] when AIDS-testing in October will take *all* energy of BTS [the Red Cross blood transfusion service] to cope with the initial problems?
[Emphasis in original.]

Dr Furesz testified that, at that time, he believed that a look-back program would be an unbearable burden for the Red Cross.

HIV-antibody testing and recipient notification in Canada

HIV-antibody testing was implemented throughout Canada by the beginning of November 1985. During October 1985, blood donations were beginning to be tested in several centres, and some were found to be HIV-antibody positive. During this same period, several transfusion recipients were diagnosed with AIDS. One might have expected that both situations would have prompted look-back and trace-back activity. That did not happen.

In December 1985, the Red Cross's Toronto blood centre conducted look-backs only in cases in which recipients of transfusions were found to be infected. Officials at that centre believed that donors who had already been proven to have infected a recipient were more likely to have infected other

recipients than were donors who had merely been found to be antibody positive. Look-backs in those cases were not immediately implemented because it was felt that there were higher priorities.

Look-backs were impeded by the inadequacy of records in many hospitals. Hospital blood banks kept records of the disposition of the components they had received, but there was no uniform requirement that such records be kept, and often records had been destroyed by the time look-backs were undertaken. Legislation in most provinces required that hospital records be kept for periods of five, ten, or even twenty years. This requirement did not necessarily mean that records sufficient for tracing the disposition of blood components would be kept. In Alberta, for example, a regulation under the *Hospitals Act* required that "diagnostic and treatment service records" be kept for ten years, but this was not interpreted by hospitals as including blood bank records. Patients' charts were kept, but they did not necessarily provide much help in identifying persons who had received contaminated transfusions. Although the fact that a patient had received a transfusion might appear in his or her chart, it would not necessarily appear in the summary of the chart or in the reporting letter to the patient's referring or family physician. As a result, information about transfusions could be obtained, if at all, only by examining the complete charts of all patients. In some hospitals, such as the Hospital for Sick Children in Toronto, records of blood transfusions were kept but were indexed only by the name of the patient. This meant that if the hospital was asked to trace a particular unit, it might have to search through all the blood transfusion files for a given year or longer. Look-backs consequently were extremely labour-intensive. Dr Roslyn Herst, the deputy medical director of the Red Cross's Toronto blood centre, wrote to hospital blood banks in the Toronto region in December 1985, asking them to change their record keeping to simplify the process of look-backs:

A number of blood banks maintain files by recipient name only. This makes it extremely difficult, if not impossible, to trace the recipient of a blood product when the Red Cross provides the unit number, the date of blood donation, and/or the date it was issued to the hospital.

The need to trace recipients of various blood products is becoming more frequent. The Red Cross is recommending that all hospital blood banks examine their method of record keeping. If it is not already in place, it is suggested that a cross-reference file of specific blood components (red cells, plasma, platelets) be kept which can be accessed by unit number and which includes data collected (from label) and which indicates name of recipient, date transfused or other disposition.

Dr Annette Poon, of the Hospital for Sick Children, responded on 20 January 1986. She said that her hospital was "aware that this system does not permit us to trace readily after one month the recipient of a particular blood

product" and that she needed a computer or more staff to institute the comprehensive filing system that Dr Herst had recommended.

Meanwhile, in the United States, the American Red Cross was performing look-backs of previous donations of donors found through testing to be HIV-antibody positive. Dr Derrick had been appointed the head of the Canadian Red Cross's AIDS Project upon its inception in 1985. The AIDS Project was a permanent project management team created by the Red Cross to deal with AIDS issues that affected the blood program. Dr Derrick learned on 5 February 1986 of the American Red Cross's procedure that was then being carried out. He made the following note in a file memorandum:

In the case of a donor confirmed seropositive for HTLV-III/LAV [HIV] being identified as associated with the development of AIDS in a blood or blood products recipient, ARC [the American Red Cross] is currently taking the following steps;

- a) determines disposition and use of any blood or blood products from the suspect donation;
- b) determines whether previous donations have been made by the same donor and when;
- c) notifies transfusion services of hospitals having association with recipients of products from suspect donation and, where the situation warrants, of products from previous donations;
- d) hospital transfusion service notifies attending physicians who will notify, as appropriate, family physician and/or Public Health Officer, depending on regional regulations;
- e) family physician will do follow-up.

The Canadian Red Cross did not adopt similar guidelines until September 1987.

For the most part, provincial and local governments in Canada made few efforts with respect to look-backs and trace-backs. The exception was in Nova Scotia, where, in December 1985, the government amended the regulations under its *Health Act* to require the Red Cross, Nova Scotia Division, to give the provincial epidemiologist identifying information about donors who had tested positive for HIV antibody. A practice developed whereby look-backs were conducted by the provincial Department of Health in cooperation with the Red Cross. The Red Cross gave the department a list of the components that had been found to come from infected donors and a list of the hospitals that had received those components. The department obtained the names, addresses, and telephone numbers of the recipients from the hospitals and then communicated with the recipients. Although it may have started as early as March 1986, the program did not begin formally until November 1986. As a result of limited resources, which hampered the program, when a recipient had moved from his or her last address, it was difficult to complete the look-back.

Early public information campaigns

Although, in preparation for the implementation of HIV-antibody testing in Canada in 1985, the National Advisory Committee on AIDS drafted an information pamphlet on the subject, no money was available from the federal government for its distribution to the public.

It was left to provincial and local health officials to distribute pamphlets to the public. Not all the information in the draft pamphlet prepared by the National Advisory Committee on AIDS was adopted by provincial and local health officials. The National Advisory Committee had recommended that "recipients of blood transfusions between 1979 and the commencement of screening of blood donations" should be "considered for testing." The Ontario Provincial Advisory Committee on AIDS, an expert advisory committee appointed by the Ontario government, produced a booklet – based on an earlier version of the draft pamphlet of the National Advisory Committee on AIDS – which did not include recipients of blood transfusions among those persons who should be considered for testing. The Ontario booklet was sent to all physicians in the province before the introduction of HIV-antibody testing. In British Columbia, a pamphlet produced by the Ministry of Health in August 1985 suggested testing only for transfusion patients with diseases such as type A hemophilia who required "frequent transfusions involving large quantities of blood and blood products."

Similar information was distributed by the Ontario Public Education Panel on AIDS, a committee created by the Minister of Health in 1985 to provide well-researched information about AIDS to the general public and to particular target groups, including young persons attending school. The panel was made up of members from organizations such as the AIDS Committee of Toronto, the Canadian Hemophilia Society, the Canadian Red Cross, and the Ontario Medical Association. In the spring of 1986, the panel produced a series of fact sheets, one of which was entitled "Detecting AIDS." Under the heading "Who Should Be Examined for AIDS?" the list of potential subjects included persons in "high-risk groups." One of the high-risk groups consisted of persons who had "received many blood or blood product transfusions since 1980 (when AIDS probably first occurred in Canada) and before November 1985 (when the Red Cross began screening blood donations)." Other recipients of blood components were not mentioned. The same fact sheet said that testing was not necessary for persons who were not in a high-risk group and had not developed any symptoms of AIDS-related illnesses. Copies were sent to all Ontario physicians, pharmacies, and hospitals.

In November 1985, given the information that was available, there was not sufficient justification for excluding recipients of blood components from the lists of persons who might benefit from testing. The Ontario message, confining the recommendation for testing of recipients to those who had received many blood or blood product transfusions, was reprinted in March 1987 and again in the summer of 1988.

Development of a policy about recipient notification

At its meeting on 16 April 1986, the National Advisory Committee on AIDS discussed a report prepared by Dr Catherine Hankins, the deputy medical officer of health for Calgary and a member of the committee. Dr Hankins urged "intensive investigation of transfusion related AIDS cases" in order to identify donors who were infected with HIV but had not yet developed symptoms of AIDS and who might be giving blood without being aware of their status. She recommended that the sexual partners of the donors and the recipients of blood or blood products derived from the donations be traced and offered counselling and voluntary testing for HIV antibody. Her report was endorsed by the National Advisory Committee on AIDS.

Two days later, on 18 April, the Ontario Provincial Advisory Committee on AIDS issued a statement and recommendations. One of the recommendations was that persons who had received transfusions between 1978 and 1985 should be informed by their physicians that they were at increased risk of HIV infection.

On 16 June 1986, an amended joint statement was released by the American Red Cross, the American Association of Blood Banks, and the Council of Community Blood Centers. It recommended that recipients of untested donations from persons who had subsequently been found to be HIV-antibody positive should be notified. The joint statement read:

Because the duration of the asymptomatic HTLV-III [HIV] infectious state is not known, it is possible that some individuals who now have a confirmed positive test for anti-HTLV-III could have been infectious at the time of a previous untested donation. If so, recipients of that untested donation could be infectious and at risk of unknowingly spreading HTLV-III infection by sexual contact, shared needles or pregnancy. For this reason, we believe it appropriate to evaluate recipients of those prior donations to identify any who might benefit from testing. If anti-HTLV-III positive persons are identified in this way, counselling about risk reduction measures may be useful for them or for their contacts.

We recommend that blood collecting establishments identify donors who now have a confirmed positive test for HTLV-III and, using existing records, begin to trace recipients of components previously donated by individuals who now have anti-HTLV-III.

The Canadian Red Cross issued a statement two days later, stating that its policy was to conduct trace-backs when recipients became infected, but not to perform look-backs on previous donations from the infected donors. It said that it would be "watching the U.S. experience carefully" to see whether it proved valuable in controlling the spread of AIDS. The statement went on to say that, based upon the number of donors who had been confirmed as HIV-antibody positive, "at most 403 recipients might be involved annually."

It noted that an apparent obstacle to conducting look-backs in Canada was that the Red Cross kept complete records for its blood transfusion centres for only one year. Because of this,

it may be necessary to recommend that anyone who received a transfusion or was treated with a blood product [between 1980 and 1985] and is concerned that this might have caused them to become infected should ask his or her physician to order a blood test.

The issues of look-back and trace-back were discussed at a meeting on 2 July 1986 of the Red Cross's transmissible diseases and immunology working group (technical subgroup). The meeting was chaired by Dr Derrick, the head of the Canadian Red Cross AIDS Project. Pat Humphreys, the director of laboratory services of the Red Cross, pointed out that, although it would be difficult, it might still be possible to trace recipients of HIV-infected blood through hospital records that were to have been kept for five years. Dr Derrick said that the issue was beyond the scope of the subgroup and should be referred back to the blood transfusion service advisory committee. He proposed

that the sub-group recommend that all recipients [of blood transfusions] since 1977 be informed of the advisability of having their blood tested for the HIV antibody and that hospitals and other concerned institutions keep track of who receives which unit for the future.

Dr Perrault, the national director of the blood transfusion service, reviewed the minutes of the meeting. He directed the subgroup to study the matter further and to prepare a position paper for Red Cross medical directors that could also be presented to the National Advisory Committee on AIDS and the Canadian Blood Committee, the blood program's funding body. In particular, the subgroup was directed to examine, first, the feasibility of a look-back and trace-back program from the perspective of the adequacy of records and, second, the feasibility and cost of informing all persons who had received blood components since 1977 about the advisability of being tested.

The matter was considered again by the subgroup on 5 September 1986. Dr Derrick said that the Red Cross was committed to taking a "best efforts" approach. He suggested, according to the minutes of the meeting, that "another possible step would be for public health authorities to contact recipients" and that, "for the sake of their contacts, they should consider having the test done." Another member of the group said that "whatever action is decided should be as low-key as possible."

On 17 October 1986, the full committee of the transmissible diseases and immunology working group discussed the issue of recipient notification. Three points were made. First, it was said that the Red Cross should wait to

see whether look-backs in the United States were successful. Second, it was said that look-backs should be carried out on previous donations from persons who were found to have transmitted AIDS, and that any blood bank that received a component from those donations should be told and should inform the recipient's physician, who would, in turn, decide whether to inform his or her patient. Third, it was said that the Canadian Medical Association should be urged to notify physicians "that they might wish to advise patients who have been transfused since 1979 and who have expressed anxiety about the possibility of HIV transmission that they request an antibody test."

By this time, the Ontario Provincial Advisory Committee on AIDS had produced a document called "Contact Tracing of Individuals with HTLV-III Infection," which was distributed by the Ministry of Health to all local medical officers of health in the province. The committee recommended that "recipients of blood, blood products and tissue" from persons found to be HIV-antibody positive be traced.

By late 1986, look-backs in the United States were well under way. A survey was conducted of some of the largest blood banks and transfusion centres, which in 1984 had collected approximately 3.7 million donations and administered approximately 325,000 transfusions. The survey revealed that 816 donors had been found to be implicated in HIV transmission and that they had donated a total of 1,771 times, which translated into 3,347 components. By the time of the survey, look-backs had been completed for 761 components. Sixteen per cent of the recipients of those components were found to be HIV-antibody positive. Fifteen per cent were HIV-antibody negative. Fifty-six per cent were dead, some as a result of AIDS, others from other causes (most often the conditions that led originally to transfusion treatment). The remaining recipients either had refused the test or could not be located. The conclusions of the study, published in *Transfusion*, a journal of the American Association of Blood Banks, were as follows:

These data suggest that by mid-fall of 1986, look-back was about one-half finished for AABB [American Association of Blood Banks] members and that there was a high mortality rate in recipients who were identified by the look-back. Recipients of components prepared from donations made later in the epidemic were more likely to have seroconverted. Finally, a small but important number of patients and physicians are unwilling to participate in the look-back process.

The National Advisory Committee on AIDS met on 4 and 5 December 1986. By this time, the original three-year term of the committee had expired. The Minister of National Health and Welfare re-created the committee, but changed its composition. No one from the Red Cross was invited to sit on the newly constituted committee. At the meeting, it was resolved that "the Minister encourage the Canadian Red Cross to follow up previous as well as current

recipients of blood transfusions" from infected donors. The resolution was communicated to the Red Cross on 16 December 1986. Upon receiving it, Dr Perrault expressed the view that the Red Cross's "loss of membership" on the National Advisory Committee on AIDS was "being exploited."

On 18 December 1986, Dr Thomas Walker, who was now the Red Cross's director of quality assurance, prepared the first of several proposed guidelines for a look-back and trace-back program. The guidelines stressed that the medical directors should determine the capability of the hospitals in their regions to track units of blood components and that the "ultimate extent of the Look-back process will be based upon this capability." These guidelines eventually formed the basis of the national look-back policy.

Public announcements to all recipients

On 18 January 1987, an article in the *Toronto Sun* appeared that said:

If you've received a blood transfusion in the last five years arrange for an AIDS test now.

That's the advice the Canadian Red Cross is giving to people who've received some of the five million pints of blood drawn from their banks in that period.

The Red Cross was displeased with this report and insisted that it be corrected so that a much less threatening message would be conveyed. The next day, the *Sun* published the following story:

The Red Cross wants to dispel any fears raised by a *Sunday Sun* story concerning blood transfusions and the risk of contracting AIDS.

A story yesterday incorrectly stated that anyone receiving a blood transfusion within the last five years should immediately be tested for AIDS.

Dr John Derrick, AIDS project director for The Red Cross, said yesterday the story raised unnecessary fears among transfusion recipients who flooded the Red Cross with calls for advice.

Derrick emphasized yesterday there is almost no chance of anyone contracting AIDS through a blood transfusion done since November 1985.

Since that time, The Red Cross has been testing blood donations for the AIDS virus and Derrick said the chance of AIDS being transmitted by transfusion is "so small it's difficult to calculate."

As for blood transfusion recipients prior to November 1985, Derrick said the chance of having been infected with AIDS is between one in 200,000 and one in 400,000.

A much more accurate estimate of risk was presented by the proportion of Canadian donors who were found to be HIV-antibody positive in the first year of testing. Between the introduction of testing in the autumn of 1985 and

31 December 1986, 236 donors had been confirmed as HIV-antibody positive by the western blot test. The rate of infected donors was 17 per 100,000. This meant that the chances of receiving a single unit of contaminated component, had there been no testing, would have been thirty-four in 200,000, and not one in 200,000 to one in 400,000 as Dr Derrick had said.

Dr Robert S. Remis, an epidemiologist, formerly the director of the regional bureau of infectious diseases in Montreal and now a consulting epidemiologist with the AIDS bureau of the Ontario Ministry of Health and an associate professor in the department of health sciences of the Faculty of Medicine at the University of Toronto, examined the incidence of transfusion-associated AIDS in Canada in a study reported in 1994. He found that in 1985 the rate of transfusion-associated HIV infection in Canada was 26.1 per 100,000 units transfused, varying between 5.0 and 66.2 per 100,000 units transfused, depending on the blood centre. It is important to remember that recipients of blood components usually receive more than one unit. In 1989, for example, the average patient transfused with red cells received 4.3 units. These figures suggest that the risk of infection with HIV was not between one in 200,000 or one in 400,000 (0.25 to 0.5 per 100,000) as Dr Derrick had said. Rather, the risk for a patient who received the average number of units of red cells in 1985 was 112.2 per 100,000, varying between 21.5 to 284.7 per 100,000, depending upon the centre at which they were transfused.

The Red Cross continued its attempts to allay public concern in 1987. In response to a U.S. government announcement, the Canadian Red Cross Society released the following statement to the press on 17 March 1987:

It was announced today that U.S. government health agencies would recommend that anyone who received a blood transfusion between 1978 and 1985 in areas where there were many AIDS cases (such as New York City and San Francisco) should be tested for possible infection by the virus that causes AIDS. The Canadian Red Cross Society is concerned that this may alarm Canadian transfusion recipients and wishes to clarify the situation as it applies to Canada.

There are important differences between the Canadian and U.S. situations. In Canada, the number of AIDS cases, adjusted for population differences, is approximately one-quarter that in the U.S. Also, very few cases of AIDS have been traced to blood transfusion or treatment with blood products in this country – only 38 as of March 9, 1987.

Everything that could have been and can be done to reduce the risk of infection by the blood supply has been done, including the introduction of donor screening in March 1983 to exclude those who might have risk factors for infection.

Nevertheless, some people who received blood between 1978 and the introduction of laboratory testing of donations in November 1985 may still be concerned that they may have come into contact with this infection as

a result of treatment with blood or blood products or for other reasons, such as sexual contact. The Red Cross advises that such individuals, for their own welfare and peace of mind and that of their loved ones, should discuss their concerns with their physician, who may recommend a blood test to determine whether or not they have been exposed to the AIDS virus.

The Ontario Ministry of Health issued a similar message, encouraging persons who were concerned about having been infected with HIV by blood transfusions to see their physicians. In a pamphlet entitled *AIDS – Let's Talk*, published in the summer of 1987, the ministry stated:

A small percentage of AIDS cases were caused by blood transfusions given before 1985 when scientists did not know the virus would be spread by blood. If you received a transfusion between 1980 and 1985, there's a slight chance you may have been infected with the virus. If you are concerned, you should see your doctor.

Look-backs at some Red Cross blood centres

The state of look-backs and trace-backs was reviewed by the National Advisory Committee on AIDS' subcommittee on epidemiology and public health, at a meeting on 4 February 1987. The subcommittee noted that previous donations by repeat donors who had been found by the Red Cross to be HIV-antibody positive were not being investigated systematically throughout the country. The subcommittee made the following recommendation:

That the local Medical Officer of Health should be informed by the CRC [Canadian Red Cross] of seropositive repeat donors requiring "look-back" investigation in their jurisdiction and should coordinate follow-up with the hospital to determine who received the potentially infected blood. The hospital should take responsibility for notifying the physicians of surviving patients identified by this system.

The recommendation was endorsed in a revised form by the full committee of the National Advisory Committee on AIDS during a meeting on 17 and 18 March 1987.

Between February and September 1987, the Red Cross, at both the national and local levels, considered and amended the look-back guidelines that had been drafted by Dr Walker, the Red Cross's director of quality assurance, in December 1986. During this period, the guidelines were considered by a series of Red Cross committees.

Early in this period, in March 1987, a look-back project in Calgary was completed. A forty-year-old man had died of AIDS in July 1986. In 1983, he had received twenty units of blood components from twenty separate

donors, nineteen of whom were located. One of the donors was found to be HIV-antibody positive. Previous donations from this person, which had been separated into twenty-five components, were traced. Seventeen components had been released to hospitals, and sixteen of them had been used. Two of the recipients had died of AIDS. One living patient, a hemophiliac, had contracted AIDS. Three additional living recipients who were found were tested and found to be HIV-antibody positive.

The results of the look-back were discussed at a meeting of Red Cross medical directors on 23 and 25 March 1987. Dr Walker was given the task of drafting a briefing paper for the Red Cross board of directors about the look-back project, and was asked to redraft the look-back guidelines. The medical directors agreed that discussions should be held with the National Advisory Committee on AIDS with respect to the issue of testing of everyone who had received blood components since 1978.

Inadequate hospital records continued to be a problem. By April 1987, it was clear that the Toronto General Hospital, the largest user of blood components in the Toronto region, was unable to trace specific units of blood components. In May 1987, Dr Herst repeated her request to hospital blood banks, first made nearly a year and a half earlier, that they keep records that would make it possible to trace units.

In mid-1987, the Red Cross still had no formal look-back policy. At a meeting of the blood transfusion service advisory committee on 12 June 1987, the look-back guidelines were discussed. Some members suggested that the Red Cross could be subject to criticism for not implementing a look-back policy sooner. Dr Derrick replied that he had publicly stated that concerned persons who had received transfusions before 1985 should consult their physicians about being tested. Dr Davey proposed that the Red Cross continue this practice. He said that a more formal look-back process was being developed and would be implemented when resources were available.

Soon after the beginning of look-backs in Toronto, it became clear that the process would be time-consuming and difficult – and in many cases impossible. In May and June 1987, a summer student was hired to search issue vouchers – which recorded the hospitals to which the donations were sent – at the Toronto blood centre to determine where potentially infected components had been sent. In three and a half weeks of work, the student was able to trace the disposition of only forty-one of 137 suspect components. Moreover, all components issued before 1985 were essentially untraceable because, until that time, the policy of the Red Cross was to keep issue vouchers for only one year. That policy had been developed to address the problem of post-transfusion hepatitis. The Red Cross believed that hepatitis had a latency period – during which a person could be infected but show no signs of the disease – of, at most, a few months. Accordingly, many cases would appear well within the one-year period during which issue vouchers were kept. The policy of keeping issue vouchers for only one year was not changed

until 1985, despite the fact that in 1984 it was known that AIDS had a latency period of at least two to five years.

The Red Cross continued to revise the look-back guidelines. A new draft was prepared on 6 July 1987, approved by the medical directors and sent to the national office of the blood transfusion service on 16 September 1987. The guidelines were as follows:

- 1.1 Look-back will be undertaken whenever a donor is identified as anti-HIV seropositive as a result of either routine screening, or investigation of a transfusion-associated AIDS case.
- 1.2 Before undertaking any look-back, Medical Directors should contact the hospitals in the Centre's service area to ascertain their capability to track units through to recipients, since the extent of a Centre's "Look-back" investigation will be limited by this capability as well as by the extent of the Centre's own records.
- 1.3 When an anti-HIV seropositive donor is identified, the donor's records will be traced back to two consecutive seronegative screening results separated by six months. If no such result can be found, records will be followed back to identify recipients, as a first step, for a minimum of two years prior to the earliest donation known to be positive.

Note: Centres may elect to "carry out" a complete "Look-Back" (i.e., to the limit of hospital/Centre records), at the discretion of the Medical Director.

- 1.4 All components of donations identified in the search of records will be accounted for.
- 1.5 Hospitals will be asked to follow-up by providing information concerning the transfusion in question to the treating physician. The treating physician should be asked to have the recipient tested for anti-HIV and to provide the test results to both the CRCS [Canadian Red Cross Society] and the hospital.

Note: The time allowed for return of information to the CRCS should balance a consideration of what can reasonably be accomplished by the hospital with the need to complete the "Look-Back" as quickly as possible in order to identify those individuals at risk of transmitting the virus to their contacts.

- 1.6 Criteria for terminating a "Look-back" are:
 - a. two donations, preceding the earliest seropositive or infectious donation by at least six months, that can be completely accounted for, with no evidence of HIV transmission, or
 - b. the limitation of hospital/Centre records is reached.

- 1.7 Steps 1.4 and 1.5 will be repeated, using a two-year time frame, until one of these criteria is achieved.

On 25 September, Dr Derrick reported about the look-back policy to the Federal-Provincial/Territorial AIDS Committee, a committee that consisted of representatives of provincial and territorial health ministries and of the Department of National Health and Welfare, including a federal assistant deputy minister, and that met to discuss AIDS-related issues of concern to both levels of government. Dr Derrick told the committee that definitive guidelines for look-back involving HIV-antibody positive donors had been developed and distributed to Red Cross medical directors, and that their use was now a standard operating procedure. The committee asked for a copy of the guidelines and a summary of look-back investigations that had been conducted. At the time, the only look-back operation that Dr Derrick knew of was the one in Calgary.

Dr Derrick told the committee that, over the previous eight to ten months, the Red Cross had consistently suggested to persons who had received blood transfusions in the five years preceding HIV-antibody testing of donations that they consider being tested if their physicians advised them to do so. In an internal memorandum dated 30 September 1987 to Dr Brian McSheffrey, who was the acting national director of the Red Cross blood transfusion service, and to Dr Walker, Dr Derrick wrote: "I believe the CRCS should consider being more pro-active in this regard if we are to compensate for the possible deficiencies in Look-back and Contact Tracing resulting from lack of records, staff to follow up and financing for such activities."

By November 1987, the National Advisory Committee on AIDS had recommended that "voluntary HIV antibody testing may be advisable" for persons who had received blood components between 1978 and 1985. On 18 November 1987, Dr Derrick gave the Federal-Provincial/Territorial AIDS Committee a written summary of the Red Cross's look-back and trace-back activities. Dr Derrick described the efforts of the 1985 trace-back in British Columbia, described it as successful, and said that similar tracing had taken place in other regions. He added, however, that it had become apparent "that these types of tracing are extremely labor intensive and often unrewarding due to lack of adequate records identifying recipients, problems with changes of address of donors and/or recipients, etc." Dr Derrick attached to the summary a chart summarizing look-backs that had been performed to that date. Of donations received before November 1985, 306 suspect donations, involving 873 components, had been checked. Sixty-four recipients had been located and tested, and thirty-one of them were found to be HIV-antibody positive.

As late as the summer of 1988, look-backs were still proceeding slowly. On 24 June 1988, the director of laboratory services of the Red Cross, Amin Adatia, wrote to Dr Blair Whittemore, who had succeeded Dr Perrault as the national

director of blood services, to say that many Red Cross centres were either failing to provide information on look-backs to the national office or had failed to investigate existing cases. He wrote that the "records indicate that out of a total of 266 Look-back cases documented, only 43 cases have been completed."

Failure of look-backs and the need for testing all recipients of blood components

In June 1988, the U.S. Presidential Commission on the HIV Epidemic recommended that hospitals develop a program to notify individuals at risk of transfusion-related HIV infection. In July 1989, thirteen months later, Dr Jo Hauser, the executive director of the Canadian Blood Committee, communicated this recommendation in a letter to Dr Clayton, the director of the Laboratory Centre for Disease Control, which acted as the secretariat for the National Advisory Committee on AIDS. Dr Hauser also reported that a blood bank in Louisiana had recommended publicly that anyone who had received a blood transfusion between 1977 and 1985 should have an HIV-antibody test. The blood bank had justified its recommendation by the fact that "recent studies presented at the Fifth International Conference on AIDS in Montreal indicate that approximately five hundred individuals in the greater New Orleans area are likely to be HIV-infected as a result of blood transfusions received between 1977 and 1985." Dr Hauser added that an article in *Blood Bank Week*, the weekly newsletter of the American Association of Blood Banks, had reported that look-back programs had identified only about 10 per cent of HIV-antibody positive recipients of transfusions. He asked whether Dr Clayton thought it "worth considering encouraging Canadians who received blood transfusions between 1977 and 1985 to have an HIV antibody test."

Dr Clayton responded that many individuals who received blood donations during that period had already been tested. He wrote that the National Advisory Committee on AIDS had recommended against mandatory or compulsory HIV-antibody testing for recipients of blood components, but that voluntary testing might be advisable. His letter continued:

If the Federal Government were to make a wide spread recommendation, it should only be done in conjunction with the provinces as they will be doing the testing, not the Department of National Health and Welfare nor the Canadian Red Cross. Further, any notification of such testing recommendations would result once more in inquiries regarding the safety of the blood supply ...

I do not believe there is any public health rationale for recommending this manoeuvre at this time. And as you say in your letter, the incidence of AIDS is much lower in Canada than the US during this period.

A widespread recommendation for testing was discussed, for the first time, at a meeting of the Canadian Blood Committee on 4 and 5 October 1989, at which Dr Hauser reported Dr Clayton's letter. The minutes of the meeting state:

The members [of the Canadian Blood Committee] recognized the potential for major public controversy on this issue. If the issue becomes public it may be felt that the public should have been informed about the risks of transfusion recipients potentially transmitting HIV infection.

Between 1989 and 1992, few efforts were made to inform recipients of blood components about the risk of transfusion-associated HIV infection.

Hospital for Sick Children study and subsequent public announcements

In the autumn of 1992, researchers at the Hospital for Sick Children in Toronto began to prepare a proposal for the targeted notification of children who had received blood components during the period between 1980 and 1985. As noted earlier, in a targeted notification a hospital identifies, from its records, patients who had received components and notifies them of this fact. The Hospital for Sick Children suggested doing so because it realized that families might be unaware that their children had received blood components and might be at risk; that HIV-infected children might show no symptoms for more than ten years after infection; that those who had received components were reaching the age at which they might be transmitting HIV to sexual partners or children of their own; and that, with the development of effective treatments and preventive measures, knowledge of infection could help persons to improve the quality and length of their lives.

The researchers determined that approximately 17,000 children had received blood components at the Hospital for Sick Children between 1978 and 1985. Rather than attempting to notify all at once, the hospital undertook a study of approximately 1,700 children who had undergone major cardiac surgery during the high-risk years to determine the most effective means of reaching former patients. It planned to communicate with patients through their physicians and to suggest to the physicians that their patients be tested. Before the physicians could be contacted, however, the news media learned of the program and reported it. The hospital decided to incorporate the publicity into the study by determining what role the publicity had in encouraging patients to be tested.

The hospital was able to communicate with 43 per cent of the approximately 1,700 children. Of those 43 per cent, it was determined that seventeen children (one of every forty-three) had contracted HIV from blood

components. Eleven of them were already aware of their condition; the other six had not been aware of their status before the communication. A high proportion of the total number of former patients surveyed, approximately two-thirds, were unaware that they had received blood components. A smaller proportion of the parents, approximately one-quarter, were unaware that their children had received blood components. Most of the former patients, although aware of the risk of HIV in the blood supply, did not connect the risk to themselves until they heard about the project in the media. Indeed, it was the media coverage that prompted more than 70 per cent of those surveyed to be tested. An overwhelming majority, more than 95 per cent of former patients and their parents in the study, were in favour of being informed of the risk.

The preliminary findings of the Hospital for Sick Children survey were presented by Dr Susan King, the lead researcher of the study, at a meeting in June 1993. The meeting was attended by representatives of the Ontario Ministry of Health, the Red Cross, the College of Physicians and Surgeons of Ontario, the Ontario Medical Association, and the Ontario Hospital Association. Two of the findings were striking. First, only a small proportion of the children who had received multiple blood transfusions had been tested for HIV antibody before the study. Second, a large proportion of children infected with HIV, approximately one-third, still had no symptoms and were unaware that they were HIV positive. The meeting agreed on the need to respond to these findings by issuing a statement to the public and to the medical profession. Soon afterwards, in July 1993, Dr Richard Schabas, the chief medical officer of health for Ontario, issued a public statement urging persons who had had surgery or a major illness requiring blood transfusions during the period from 1978 to 1985 to speak to their physicians about being tested for HIV antibody. The statement went on to say that, although the risk was small, physicians should encourage patients to be tested.

Ontario's announcement and the findings of the Hospital for Sick Children study attracted much publicity. The effect was readily apparent in the number of persons who sought testing. After the press reports of the hospital's study in April 1993, the number of blood samples submitted to the Ontario Public Health Laboratory for HIV-antibody testing increased from slightly more than 600 per day to more than 1,200 per day. By the middle of May, the number of samples submitted to the laboratory had returned to the normal level. In July 1993, after Dr Schabas's announcement, the number again climbed to approximately twice the normal average.

Most provinces followed Ontario's lead in making a public announcement. New Brunswick undertook a campaign on 26 July 1993 with a public announcement, followed by newspaper advertisements ten days later. British Columbia, Saskatchewan, and Quebec issued similar announcements in

September 1993. Saskatchewan had previously, in September 1992, sent a pamphlet to physicians that stated that persons who had received blood or blood products between 1978 and 1985 should be considered for testing. Nova Scotia released a ministerial statement in November 1993 outlining the results of the Hospital for Sick Children study.

In Manitoba and Alberta, there was political reluctance to issue public statements encouraging testing. In Manitoba, senior public health officials had sought a public announcement as early as July 1993. In October 1993, still without authorization, the chief medical officer of health made a public announcement advising persons who had received blood components between 1978 and 1985 to be tested. In Alberta, despite the urging of senior public health officials that the government issue an "advisory" to the same effect, the Cabinet refused to authorize such a notice until November 1993.

The stored samples

During the mid-1970s, the Red Cross's Toronto blood centre began storing frozen samples of blood donations for approximately six months. The purpose was to assist in tracing cases of post-transfusion hepatitis. From 1 December 1984, samples were retained permanently. In early 1994, during the Inquiry, it was revealed that approximately 175,000 of these samples, taken from blood donors between 1 December 1984 and 31 October 1985, were still in existence. They had not been tested. If they were tested, and if any that proved HIV-antibody positive could be linked to recipients of blood components from those donations, it might be possible to identify HIV-infected persons who would otherwise be unaware of their status.

In April 1994, the Red Cross formed an expert advisory committee consisting of seven independent persons, representing a variety of interests and disciplines, to advise it what to do with the samples. The committee reported in August 1994. The committee estimated that between 154 and 531 donors, recipients, and sexual partners of donors or recipients could be infected and traceable from the frozen samples. Of those, between thirty-four and 115 would still be alive and between eighteen and fifty-nine would be infected and unaware of their condition. The expert advisory committee concluded that "there was an ethical requirement to test the samples in order to allow affected transfusion recipients to be warned that they had been exposed to HIV."

In the autumn of 1994, the Red Cross undertook a program of testing the samples. This program represented the first effort to test the samples and undertake look-backs. The number of positive samples was less than the number estimated. Twenty-two donors were identified as HIV-antibody positive. Of these, only nine had been previously known by the Red Cross to be HIV-antibody positive.

Commentary

The notification of persons potentially infected with HIV through blood components ought to have been a high priority of the Red Cross, hospitals, and public health officials. Without knowledge of their infection, these persons were denied the opportunity of preventing infection of their sexual partners and of any children who might be conceived. They were also denied the opportunity of seeking treatment. Every infected person unaware of his or her condition could, moreover, infect others by donating blood. Given what was known about the infectivity of HIV through blood components and the latency period of the disease at that time, there should have been no doubt, from the summer of 1984 onwards, that there was a significant number of persons who had been infected with HIV from blood transfusions and who were unaware of their condition. Despite the clear urgency to inform those persons and to protect others who might be infected through them, the measures that were adopted were neither timely nor effective. This was an urgency that was apparent at the time.

With the exception of Nova Scotia, no leadership was taken by provincial governments to encourage or facilitate look-backs and trace-backs. There was little formal communication between Red Cross blood centres and public health departments about the names of persons infected with AIDS or HIV. There were few, if any, government measures to encourage or require hospitals to keep records of transfusions that would have made it possible to locate recipients.

The federal government disregarded invitations for it to act. In July 1985, the Bureau of Biologics characterized the issue of notification as one of "ethics" best left to professional societies. For its part, the Laboratory Centre for Disease Control did not encourage physicians to report cases of AIDS and HIV as it had done for toxic shock syndrome. Nor did it encourage physicians to inform the Red Cross about patients diagnosed with AIDS who might donate blood. Although it was not required to do so, the Laboratory Centre for Disease Control could have taken a position of leadership and encouraged provincial public health departments to give the information in their possession to the Red Cross.

As a result of the lack of government leadership, the Red Cross was largely left on its own to address an issue for which it was ill-equipped and insufficiently motivated. The Red Cross had never communicated with recipients of blood products. It had no records of its own to trace blood components after they had reached the hospital. It had no power to compel hospitals to keep appropriate records of the use of blood components, nor could it compel public health authorities or physicians to give it information about persons with AIDS and HIV.

That the Red Cross was insufficiently motivated to engage in look-backs is evident in the fact that it did not begin to develop a national policy about look-backs and trace-backs until the summer of 1986. The development of

that policy then took more than a year, and after it was developed the national policy was not carried out in a timely way. Instead, the issue of notifying recipients of potentially infected blood components proceeded through the convoluted committee structure of the Red Cross that had previously proved so ineffective in dealing with such other AIDS issues as the preparation of the donor-screening pamphlet. By the summer of 1988, a full year after the policy was developed, and nearly three years after the implementation of testing, only approximately 20 per cent of documented look-back cases had been completed.

In the notification of recipients, Canada trailed significantly behind the United States. Look-backs were well under way throughout the United States in 1986. By contrast, a national look-back policy was not in place in Canada until the autumn of 1987. It is important to note that U.S. blood bankers and public health officials have been criticized by their country's Institute of Medicine for failing to develop a look-back policy earlier. The Institute of Medicine also found it "peculiar" that recommendations by the U.S. Food and Drug Administration about donor deferral in 1983 contained no recommendations concerning recipients of blood products derived from persons subsequently found to be infected. The institute concluded that there was abundant evidence by 1985 to justify "a vigorous stance about look-back." No comfort can be taken from the fact that, with respect to this important public health problem, Canada was "only" a year behind the United States.

The difficulty of conducting effective look-backs, not least because of the inadequacy of hospital records, but also because of the mobility of donors and the amount of time that had elapsed, was obvious by 1988. One might have expected those difficulties to have encouraged the Red Cross and public health officials to find alternative means of notifying recipients of potentially infected components. In particular, it should have seemed obvious that communication to the recipients of blood components, either directly or through the mass media, could be an effective means of identifying those who were infected. However, few efforts were made to do so until the early 1990s. In particular, public statements made by the Red Cross, advising those concerned to consult their physicians, appear to have been aimed more at allaying fears than at communicating useful information to potentially infected persons. Government officials appear to have been more concerned about preventing public questioning about the safety of the blood system and about deflecting controversy than about informing persons who might be infected. It was only when government officials were met with the findings of the Hospital for Sick Children study in 1993 and the ensuing publicity that they acted in an appropriately assertive manner.

3538

